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# SELECTIONS

FROM THE

# DERMATOLOGICAL WRITINGS

OF

# DR. P. G. UNNA. 1850-

TRANSLATIONS, CHIEFLY IN ABSTRACT.

EDITED BY

PHINEAS S. ABRAHAM, M.A., M.D., B.Sc., F.R.C.S.I.,

LECTURER IN PHYSIOLOGY AND HISTOLOGY, WESTMINSTER HOSPITAL MEDICAL SCHOOL; PHYSICIAN TO THE WESTERN SKIN HOSPITAL, LONDON; AND EDITOR OF THE 'JOURNAL OF THE LEPROSY INVESTIGATION COMMITTEE.'

# PREFACE.

Dr. Unna's contributions to dermatological literature are so numerous that, with the space at disposal, translations or abstracts of only a few could be included in this volume. The editor, indeed, is quite aware that several important papers by the author will not be found in the series; and he wishes to state that, with one exception, the selection has been taken from a number of reprints which Dr. Unna himself sent to the Secretary of the New Sydenham Society for the purposes of this work. A complete list, however, of the author's publications is appended. The translations are, for the most part, given in abstract.

The Editor desires to record his thanks to Dr. Chichester May, and Messrs. H. Felkin and A. D. Abraham, who have materially helped him in preparing the translations and abstracts; and to Dr. Alfred Eddowes, who is responsible for the article on Favus.

The proofs have been submitted to and kindly approved by Dr. Unna.

P. S. A.

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# LECTURES

ON THE

# GENERAL PATHOLOGY OF THE SKIN.

DELIVERED IN THE WINTER SESSION, 1888-89.[1]

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## I. Anæmia.

The vessels of the skin undergo greater changes of calibre within physiological limits than do those of any other organ, and this is due to the great development of its muscular and nervous apparatus. In its pathology, too, contraction of the vessels plays an important part, but here other factors are also at work in producing anæmia, viz. qualitative and quantitative changes in the total amount of blood in circulation. If the anæmia be caused by contraction of vessels, the skin feels cooler and often less succulent; but if the tone of the vessels remain normal, the temperature and the amount of fluid in it may be as before, although it may be anæmic. Hence anæmia of the skin may be divided into two great groups: (1) Anæmia due to general alterations in the total quantity of blood, and (2) Anæmia confined to the skin.

Anæmia consequent on qualitative blood-changes may be due to a deficiency of red, or an increase of white, corpuscles, or to a combination of both factors. A want of red corpuscles makes the skin and mucous membranes anæmic in true chlorosis, in acute and chronic inanition where the

[1] "Vorlesungen über allgemeine Pathologie der Haut, gehalten in Wintersemester," 1888-89—'Monatsh. für prakt. Derm.,' ix Bd., 1889, Nos. 1, 2, 6, 8, and x Bd., 1890, Nos. 3, 4, 6, 7—I. Anämie.

patients cannot take food, in those recovering from consuming febrile diseases, in pseudo-leukæmia, and in hydræmia; but in leukæmia there is also an absolute and relative increase in the number of the white corpuscles, and in certain forms of anæmia and cachexia—*e. g.* in absolute starvation and advanced tuberculosis and cancer—in addition to a deficiency of hæmoglobin, there is also a diminution in the total quantity of blood. Not only is there here a change of colour of the blood, but there is an adaptation of the vessels of the skin to the diminished supply, *i. e.* the stream-bed of the skin becomes contracted in simple diminution of the blood. This is seen, too, after loss of blood from wounds and operations, and in cases of intestinal parasites, as in pernicious anæmia. After severe hæmorrhage in young persons, the skin becomes waxy, yellow, and transparent, from the regulative contraction of all the vessels of the skin and absorption of tissue-fluids by the veins and lymphatics.

The ashy-grey colour of the skin in cholera is similarly due to a general contraction of the cutaneous vessels, combined with increasing cyanosis of the blood, as the velocity of its current diminishes. The fall of temperature and increase of the vascular tone of the skin resulting from these quantitative anomalies of the blood, approximate such cases to the isolated anæmia, which we shall now consider, and in which qualitative changes are of course excluded. This anæmia may involve the whole skin or only parts of it. When the whole skin is anæmic, either the circulation in general or the central nervous system must be affected. Contraction of the cutaneous arteries always runs parallel with the anæmia, and sometimes this contraction follows a diminished blood supply; but whether the arterial constriction or the diminution of blood in the skin be primary in any given case, is often as difficult to determine as in physiological experiments. Arterial constriction is certainly primary in the death agony, and it causes that unfortunate pallor which makes the *post-mortem* study of most dermatoses so difficult, and that of the circulation anomalies impossible. The paleness accompanying cardiac weakness, especially that which precedes fainting and obviates a dangerous fall of blood-pressure, is also probably primary in nature. To the

same category belongs the anæmia which accompanies or precedes nausea (*ab injectio medicamentis*, chloroform, swinging, and sea-sickness), and in which there is often an accompanying inhibition of the splanchnics, causing plethora of the intestinal tract, the anæmia of the skin being here regulative. Reflex spasm of the cutaneous arteries is also often caused by the prodromata of an epileptic fit, by psychical disturbances (fear, sudden terror), and by strong stimulation of sensory nerves, especially of the abdomen, as in colic. The goose-skin due to mental perturbation indicates, moreover, powerful stimulation of all the unstriped cutaneous muscular tissue, including the vascular.

A secondary adaptive contraction of the dermal vessels gives rise to the pallor following night-watching and excessive muscular or cerebral activity, when there is a collateral overfilling of the vessels of internal organs, according to their needs.

The most important example of a general contraction of the cutaneous vessels is seen in the signs of all acute infective diseases. Here the poison circulating in the blood supplying the vaso-motor centres, gives the stimulus which results in the periodic contraction of the peripheral vessels. If the rigor be severe the vessels of the superficial muscles are also affected, and those of the internal organs become abnormally full. Hence the temperature of the surface falls, and that of the deeper parts of the body rises. Influences which paralyse the vessels, such as warmth, can partly overcome their tonic contraction. As is well known, during the rigor the temperature of the closed axilla is already rising. On the other hand, cold accelerates the rigor, showing that the tone of the vessels, in the interval between the rigors, is really raised, and only kept in check by the greater warmth of the blood and the increased cardiac action.

Certain organic poisons, especially strichnine and ergotine, increase the tonic contraction of the peripheral vessels, although there is not the arterial spasm of rigor; and the pallor after acute poisoning with alcohol is similarly produced, by the products of its decomposition.

It thus appears that it is not a slight irritation which causes, reflexly or directly, a general cutaneous anæmia, but

pathological circumstances which attack profoundly the whole constitution. This is easily understood when we consider that the normal constriction of the vessels is considerable, and that the vaso-motors must be intensely stimulated in order to produce universal visible pallor and sensible cold. We may, therefore, safely ignore a paralysis of the dilators in the production of general cutaneous anæmia.

In contradistinction to the general causes which produce universal anæmia we have to look for local causes for the production of localized anæmias. These can be more easily classified into those due to primary vascular constriction, and those in which the narrowing of the calibre of the vessels is secondary to a diminished blood supply.

We make frequent use of the latter principle, and increase the vascular tone; for instance, when we raise the extremities to an unwontedly high position, for the purpose of quieting the circulation or lessening pain.

Ligaturing an artery causes immediate contraction of its trunk and branches on the distal side of the ligature, and in the case of a vein, on the proximal side as far as the first collateral branch; and the contraction accurately represents the pressure of the column of blood which has been removed. Perceptible paleness is rarely produced in these cases—only temporarily, indeed, even after ligaturing a large artery such as the femoral, for the collateral circulation is soon established. The anastomoses of the superficial and deep cutaneous networks of vessels are far too extensive for the ligaturing of a few of them to make any impression on an area of skin.

A partial emptying of the vessels through external pressure is another cause of local anæmia. The compression may be from without the body, as from the finger, articles of dress, bandages, &c., or from within, from tissue masses, &c., beneath the cutis. While arterial ligature generates localized anæmia with difficulty, pressure on the arterioles and capillaries produces it with ease, but only so long as the pressure lasts; on its removal, the anæmia is replaced by a relaxive hyperæmia—the vessels having become paretic through the pressure. In this manner, too, act tumours of recent date which stretch the skin, collections of fluid and foreign bodies, as well as rapidly growing abscesses, temporary œdemas,

injections, and urticaria. But if the pressure on the cutaneous vessels has lasted for weeks or longer, as in atheroma, uric acid concretions, chronic œdema, myxœdema, tumour-like infarcts of the lymph-spaces, such as occur in dermal leprosy—an organic narrowing of the vessels takes place, the whole cutaneous vascular network is diminished, and many capillaries are obliterated. Further on we shall see that this is the cause of many forms of anæmia; the skin remaining pallid and anæmic, like a cicatrix, after pressure has been removed and swelling has subsided.

Local anæmias, due to primary arterial constriction, may be subdivided into those arising from spastic contraction of the arterial muscle-tissue, and those due to an organic narrowing of the vessels. The former, of course, are generally temporary, and the latter permanent; but a spastic narrowing may occasionally last for some time—hence it is best to retain the division just mentioned. A classification based on a narrowing of arteries on the one hand, and on a contraction of capillaries on the other, however useful in single cases, cannot be generally maintained; for, although every narrowing of capillaries is not due to arterial constriction, the lessened calibre of an artery always results in a capillary narrowing, at any rate in the stretched elastic skin.

Cold is the commonest cause of increased tone in the cutaneous vessels; but to produce the effect the cold must be considerable, as from an ice-bag or ether spray. If the difference of temperature between the cold body and the skin be inconsiderable, or the abstraction of heat be made difficult in any way, the temporary arterial spasm, in healthy individuals, is followed by a paresis of the vessels, and the heat may continue to be lost. This is the case when the body is submitted to a cold stream of air, or immersed in a moderately cold bath. In fact, there is a subjectively pleasant relaxive hyperæmia, the vessels being expanded beyond their normal calibre, and thus the skin is rendered to some extent inert to the heat-abstracting agent, the increased flow of warm blood compensating with accuracy the loss of heat.

The effect of slight cold, such as normally acts on the exposed parts of individuals dwelling in northern countries,

thus does not produce anæmia, but a slight hyperæmia of the exposed skin—the result being what we call a fresh, healthy colour. On the other hand, the inhabitants of warm countries have the face and hands normally pale—like the covered parts of those living in cold climates. The pale face and hands of southerners, and the pale bodies of northerners, do not generally show the reflexly produced pulsating hyperæmia : we have evidently here to do with a greater normal contraction of the vessels; and we shall probably be right in regarding this increased tone as compensatory to the relaxing effect of warmth on the cutaneous vessels, just as we formerly considered red cheeks as produced by an action compensatory to the effect of cold.

In spite of this, the inhabitants of warm countries are not anæmic, it is only that their cutaneous vessels have contracted in a regulative manner. No doubt this is a purely peripheral condition, an idiospasm of the vessels, and its importance will become evident when we are considering the pathological departures from the normal.

To this class of anæmias, due to self-regulative contraction of vessels, may be added that of limbs which have been paralysed for a considerable time. This has been a bugbear to pathologists, for a paralysis of the dilators could scarcely produce recognisable anæmia; and, on the other hand, paralysis of the vaso-motors ought to produce hyperæmia; and even if this hyperæmia be transient, it would at the most give place to the normal condition, and not to anæmia. In consequence, however, of the paralysis, not only would relaxive hyperæmia occur, but later on there would be a constant hyperæmia of stagnation from the defective muscular movements, and the now greater effects of gravity. We shall not go far wrong, therefore, in considering the anæmia, which is certainly there, to be due to a peripheral self-regulation, or an idiospasm, of the vessels, which counteracts the effect of gravity and the loss of action of the voluntary muscles. This explanation is rendered more probable by the fact that paralysed limbs become not only anæmic but often œdematous, from an increase of venous as well as of arterial tone, a phenomenon which has not hitherto been satisfactorily explained, but which can be easily understood by

assuming it to be a part of the peripheral self-regulative arrangement.

The following instances of arterial spasm cannot be regarded, like the above, as within physiological limits. Hemicrania spastica and Raynaud's disease of the hands and feet are truly morbid affections of the tone of peripheral arteries. The former need only be mentioned here, because pallor of the skin is of course one of its characteristic symptoms; for the rest, it comes among the diseases of the vascular and nervous systems. Raynaud's disease, however, demands special consideration.

In the mildest form, found especially among washerwomen, the hands and feet, particularly the digits, are only very anæmic, and in some cases bluish white. In the cold, shooting pains occur, which rapidly pass off, and when the patients are warm in bed, or immerse the extremities in warm water, itching sensations are felt. The temperature is objectively lowered, and the tactile and temperature senses are dulled. Long-enduring anæmia of this kind can, of course, only develop where all the arteries of a given area are uniformly and synchronously narrowed; and, as we should expect, the extremities alone are attacked by this disease—for in them alone can a peripheral cause easily affect all the cutaneous vessels in such a manner that compensation becomes impossible within the area. That the branches of the cutaneous arteries, and not their trunks, are affected is proved by the normal condition in which we find the ulnar and radial arteries of the upper limb and the dorsal and plantar of the foot. It is also obvious that even the most profound anæmia is not followed by any hæmorrhagic venous accumulation of fluid—terminal arteries in Cohnheim's sense do not exist. The only effect on the circulation, beyond the narrowed arteries, is a profound anæmia of the capillaries and veins, with corresponding fall of pressure and of velocity of the blood current. The capillary stream-bed is doubtless diminished *ad maximum* by the same cause, and this may be the reason why the permanent specific anæmia of these cases does not lead to a damaging of the vascular walls—such as always occurs after prolonged mechanical constriction of an artery, and which might be expected here, seeing that the contraction

often passes off for a time. But no trace of such damage, or of hæmorrhagic œdema, is to be seen after reducing the contraction by hot bathing. On the other hand, one effect is never absent in severe cases of true Raynaud's disease, viz. a partial necrosis of the skin, which always takes place at the balls of the toes and fingers, and bed of the nails, where a compensating circulation from deep-lying vessels is quite impossible: in some cases this goes on, in the course of years, to successive necrosis of all the phalanges. The primary cause of this peripheral idiospasm is quite unknown; cold, of course, is the most important assisting influence; and not only in this respect, but in its whole aspect, this disease has many analogies to the so-called "frost-bite," which is a sort of spastic, stagnating dermatosis.

Before considering the true organic narrowing of the cutaneous arteries, we may shortly discuss the anæmia artificially produced for therapeutic or cosmetic purposes. The conditions demanding such treatment, may be either real morbid processes accompanied by hyperæmia, or their erythematous remains, or simply redness of the face and hands, which is still within physiological limits.

In these cases, stimulation of the vaso-motor nerves and vascular ganglia would be of little use, for the effect would soon pass off, and be followed by an undesirable paresis of the muscular tissue of the vascular walls; the means we possess, moreover, for producing this effect are very few. It is, however, easy to produce a diminution of the hyperæmia by the intelligent use of the group of reducing, oxygen-binding remedies. The following substances possess a chemical action of this kind, viz. sulphur and its preparations, pyrogallol, resorcin, ichthyol, and certain metals and oxides—mercury, oxide of zinc, and oxide of lead. The arterial constriction thereby produced is not rapidly generated and evanescent, but slowly developed and permanent; and is most nearly allied to organic narrowing, or thickening of the vascular walls, by the growth of young connective tissue; but up to the present, its nature is not accurately known. Since the lessening of the hyperæmia is always accompanied by diminution of any concomitant inflammation, we must probably regard it as an organic reduction of volume

of the whole vascular tree—the vascular pores being diminished and the outbreak of inflammation thus made more difficult. The thickening of the walls of the valved arterial branches of the frog's web, as described of Klemensiewicz, when the blood-pressure is falling, offers an acceptable physiological parallel.

In the really organic diminution of calibre of the cutaneous vessels, the capillaries, many of the arterioles and venules, and some few larger branches, are actually converted into cellular or fibrous connective tissue. Embolism and thrombosis, as causes of anæmia, play an important rôle in dermal pathology; but on account of the very frequent anastomosis of the cutaneous vessels, only infective embolisms have serious results. Innocent emboli, indeed, may be carried and lodged in the cutaneous network without producing symptoms, and the same is true for local thrombosis following such emboli. Careful search would no doubt reveal them, in cases of general embolism, to be much more frequent in the skin than is commonly supposed. We often find, quite unexpectedly, in the examination of tumours, thrombi of apparently harmless bacteria, of secondary importation, or hyaline thrombi in wider areas, the former being too small, and the latter allowing the blood-stream too much room, to produce any perceptible anæmia, although they must obviously increase the resistance to the blood entering the capillary area.

For the production of real anæmia, there only remains a narrowing of the capillary region, leading to obliteration of lumen by young connective tissue. The process called *endoarteritis obliterans* by Friedlander, is of much greater importance in the pathology of the skin than we might suppose. This fibrous vascular degeneration does for the skin, what the embolic and thrombotic closure of the vessels does for other organs in producing anæmia. A review of the diseases of the skin will show that it may follow infective inflammations as well as ulcerative processes, and progressive as well as retrogressive disturbances of nutrition. Without enumerating all the individual instances, we may point out the general characteristics; and for this purpose it seems appropriate to distinguish two kinds of obliterating closure of vessels. In some cases, the cutaneous vessels are oblite-

rated from the capillaries backwards, after being extremely narrowed for some time by external pressure. This atrophy, due to pressure, follows abnormal stretching of the muscular and elastic tissue of the skin, as in cases of long-standing scleroderma, pruriginous eczema, and ichthyosis, as well as in cases of prolonged pressure from atheroma, uric acid concretions, and chronic œdema. Obliterating atrophy, after thinning of the vessels by traction, we find in cicatrisations, and especially in the *striæ gravidarum*.

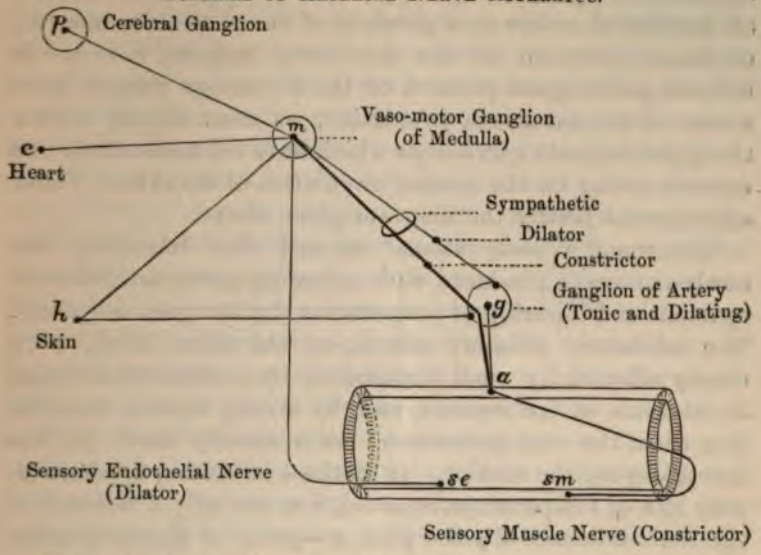
Syphilitic processes, on the other hand, cause a peculiar affection of both the larger and the smaller vessels—but chiefly of the former, in which a more or less cellular connective tissue is developed within the lumen, from the endothelium. Proceeding as it does with sclerosis of the already existing connective tissue, the production of large anæmic tumours of cartilaginous hardness may be the result. Anæmia *liodermia* may be similarly produced, but without sclerosis of the connective tissue, in the extremities of certain patients with tabes; and, in the same way, are initiated changes which lead to a whole host of fibrous hypertrophies and atrophies, as in sclerosis of the skin, morphœa, and keloid. In all these cases there has been no preceding pressure or traction; the obliteration of the vessels does not follow but precedes the existing anæmia.

## II. General Considerations concerning the Hyperæmias of the Skin.[1]

The various anæmias of the skin are, upon the whole, of a very uniform character, because in them there is no very great departure from the normal state of the circulation. The general term hyperæmia, on the other hand, includes conditions differing considerably from one another, and to understand them clearly it is necessary always to have the physiological facts of the cutaneous circulation in one's mind. The appended diagram indicates the nerve-tracts concerned in the regulation of the blood-flow through the skin.

[1] "Allgemeines über Hyperämien der Haut"—'Monatsh. f. prakt. Derm.,' ix Bd., 1889, No. 2.

DIAGRAM OF ARTERIAL NERVE APPARATUS.




The tube in the diagram represents a piece of muscular cutaneous artery, just where it is about to enter the *cutis vera*. The lines represent nerves, the circles with dots in their centre, ganglia, and the points, nerve terminations. Two terminals are within the muscular wall of the artery, a motor at *a* and a sensory at *sm*. On the internal surface of the tube is a sensory endothelial nerve, *se*. The vascular ganglion *g* gives off two nerves to the motor terminal *a*, the fine filament *g a* taking origin from it, and a thicker so-called vaso-motor, *m a*, which only passes through it. This ganglion also receives *h g*, a centripetal sensory nerve from the skin, and a centrifugal branch of communication, *m g*, from the higher centre *m*, or a so-called dilator. The vaso-motors and dilators generally run together in the case of the skin, *e. g.* the sciatic carries those for the leg. The centre *m* represents a series of vaso-motor ganglia distributed along the medulla and cord. In addition to the nerves already mentioned, branches are received by this centre *m* from the cerebrum (*p*—*m*), from the heart (*c*—*m*), from the skin (*h*—*m*), and from the endothelial coat of the vessel (*se*—*m*), each of which conveys a psychical or sensory stimulus from the organ in question. If we wish to ascend from the favoured

alternative—by which all hyperæmias, without distinction, are attributed, either to a paralysis of the vaso-motor nerves, or to an irritation of the inhibitory (dilator) nerves—to definite pathological pictures of the so various clinical anomalies of the cutaneous circulation, we must shortly review the physiological experiments which have led to the doctrines current to-day on the normal circulation of the skin. These experiments justify the diagram given above.

Ostroumoff's observations[1] showed that tetanising the newly-cut nerve produced with certainty great arterial constriction and lowering of temperature (by the tract *m*—*g*—*a*). The inhibitory (dilator) nerves, on the other hand, were chiefly affected by weak stimulation, by rythmic stimulation at intervals of five seconds, and by strong tetanic stimulation when the vaso-constrictors were already dead (on the fourth day for the sciatic). In all these instances, hyperæmia, with rise of temperature, resulted, *i. e.* not only a removal of the tonic influence (by the path *m*—*g*—*a*) of the vaso-motor centre, but also an inhibition (*m g*) of the spontaneous action (by the path *g*—*a*) of the vascular ganglia, and hence a maximum dilatation. The nature of the conditions justifies the conclusion that the dilatation is not due to an independent muscular action of the artery (Exner), but to an inhibition of all vaso-constricting influences at the peripheral ganglion, which is the point best suited for this purpose. For, with this assumption, we can understand how it is that weak stimuli produce an effect so prodigious as the removal of the contraction of the strong circular muscular fibres of the arteries; further, that rhythmic, *i. e.* cell stimuli, are particularly effective; and that after commencing degeneration of the vaso-motors a still further dilatation must ensue, since now by strong stimulation of the inhibitory fibres, which probably degenerate just as quickly, only inhibitory impulses can be started in the ganglia. By mapping out the path *m* to *a* in the way shown in the diagram, we avoid having to assume two different kinds of nerves with antagonistic muscle apparatus in the artery, for which the histology of the cutaneous vessels gives us no warrant. Neither do we

[1] "Experiments on the Inhibitory Nerves of Cutaneous Vessels," 'Pflüger's Archiv,' 1876, p. 219.

introduce unnecessary complications; for peripheral ganglia, with the definite function of inhibition, we must assume to exist in the skin in any case. It is a well-known fact, noticed by all experimenters alike, that after section of all nerve tracks connecting the vessels with the central organ, the vessels gradually contract again, and acquire new tone, which, however, never regains the old delicacy in reacting to external stimuli or the former resistance. The contraction can be explained by introducing between the passive stretching of the muscle tissue by the blood-pressure and the contraction of the muscle, a sensory element, *sm*, which, stimulated by the stretching of the muscle, leads the latter to contract (by the path *sm—a*). An independent tone, admitting of regulation within narrow limits, can, however, be established only by peripheral ganglia. According to our diagram, *g* remains intact, exercising an independent influence by the path *g a*, and counteracting the stretching of the vascular tube by the blood-pressure. The further reaction of the centrally paralysed cutaneous vessels, compared with that of unparalysed vessels, shows us how to decide with certainty by what paths the remaining active stimuli must travel. Ostroumoff found that nicotine poisoning, or poisoning by $CO_2$ (by suspending artificial respiration), only produced cutaneous hyperæmia when the nerves of the vessels were untouched. These stimuli hence travel by the path *se—m—g*, if we assume that the poisoning starts from the blood itself; or by the path *m—g*, if it affects the vaso-motor centre directly. Only very severe nicotine poisoning also dilated the vessels paralysed from their centre. Must we therefore also assume a direct path *se—g*? Probably not, for this paralysis may be looked upon as a direct action of the poison on the terminal of the tract *g—a*, independently governed by the vascular ganglion.

Latschenberger and Deahna[1] found, moreover, that centripetal fibres run from all vessels, and that their stimulation causes dilatation in the vascular area of the artery, and tends to lower the pressure which has been raised by arterial constriction in a self-regulative manner. These impulses travel by the path *se—m—g*. Starting with the proof of such

[1] 'Pflüger's Archiv,' 1876, p. 157.

sensory vascular depressor nerves, and reasoning by analogy, these authors assume the existence of similar sensory antagonistic constrictor fibres, which, when the vessels are dilated, produce a regulatory contraction by stimulation of the vaso-motor centre. This path, *se—m—a*, constructed, as it were, for the sake of symmetry, may be considered superfluous, since its existence is not proven. We can conceive the same effect to be produced in a simpler manner—by the expansion of the vascular tube stimulating directly the sensory nerve-endings situated in the stretched muscle-tissue, and thus reflexly causing a degree of contraction corresponding to the amount of expansion. We then have need only of the path *sm—a*, which we have already used to account for the vaso-constriction after section of the vaso-motors, to explain, without making use of the centres in the cord, all those cases of constriction which originate from the interior of the tube itself.

This assumption of only two kinds of sensory nerves in the vessels, viz. endothelial- and muscle-nerves, suffices for all experimental as well as pathological facts hitherto observed. The former, stimulated by pressure of the blood or of the vascular wall, produce contraction reflexly through the cord centres; the latter, stimulated by the stretching or tension of the vascular wall, cause a muscular contraction purely peripherally and directly. The gradual rise of pressure, increasing and diminishing rythmically with the heart-beat, is the natural stimulus of the inhibitory ganglia, by the path *se—m—g*, and it produces the dilatation of the arteries. The rapid and maximum expansion of the arterial wall, which occurs during arterial blood transfusion, leads (by the path *sm—a*) to so energetic a reaction in the direction of constriction, that complete occlusion of the arteries may result (Cohnheim).

The gradual constriction of the cutaneous arteries when blood-pressure is falling (*vide* Anæmia) occurs without pressure on, and stimulation of, the sensory nerves (*se*), and is therefore chiefly due to the toxic action of *m* and *g*, which accommodates the tension of the arterial wall to the diminished internal pressure. The investigations of Bernstein,[1]

[1] 'Pflüger's Archiv,' 1877, p. 575.

on the other hand, have shown that the experimental production of arterial dilatation is very much facilitated by a previous strong constriction, such, *e. g.*, as is caused by cold.

The production of anæmia by cold, the blood-pressure being normal, accumulates, by compressing the endothelial nerves *se*, a latent stimulus for the inhibitory nerves; and this becomes manifest when weak and otherwise ineffective stimuli are superadded. We have, moreover, already seen that the pallor due to external cold easily passes over to hyperæmia in the case of the healthy skin (normal reaction of cold). This happens even when the blood-pressure is only a little raised, as, *e. g.*, during quick awakening. It may also be caused by sensory stimuli, such as gentle rubbing of the skin. All these events hence occur through the intermediation of the path *se—m—g*, and, as far as we can see, the assumption is sufficient of sensory endothelial nerves which are at the same time dilators, and of sensory muscle-nerves which are also constrictors of the cutaneous vessels. The former may be considered to be identical with the nerves seen by the author and by Bremer.

We have to thank the experiments of v. Bezold,[1] and of Ludwig and Thiry,[2] for our knowledge of the fact that stimulation of the central end of sensory nerves causes rise of blood-pressure, and that the latter is the result of the contraction of peripheral arteries. This process takes the path *h—m—a*. Heidenhain,[3] much earlier, had observed a rise of temperature, *i. e.* dilatation of the cutaneous arteries, to follow stimulation of sensory nerves; and this was not obtained after section of the vaso-motors. Snellen and Loven[4] found, further, that stimulation of the central end of the auricular dilated the arteries of the ear, and that stimulation of the dorsal nerve of the foot dilated the saphenous artery. A sensory stimulus thus caused dilatation of the cutaneous artery supplying the same region, *i. e.* a reflex travelling by the path *h—g*. Finally, Goltz and Ostroumoff observed a rise of temperature, or arterial dilata-

[1] 'Untersuchungen über die Innervation des Herzens,' Leipzig, 1863.
[2] 'Sitzb. d. Wiener Akademie,' 1864.
[3] 'Pflüger's Archiv,' 1870, p. 504.
[4] 'Sitzb. d. Sächs Akad. d. Wissensch.,' 1866.

tion, even of the opposite, but symmetrical, region, after sensory stimulation. This would correspond to a stimulus taking the path *h*—*m*—*g*.

The changes of cutaneous circulation, due to the stimulation of sensory end-organs in the skin, come then from impulses travelling either by sensory cutaneous nerves directly passing to the vascular ganglia of the same region, or by cutaneous sensory nerves connected with the vaso-motor centres of the cord, through which symmetrically situated cutaneous arteries are affected.

The commonest example of stimulation by the direct path *h*—*g* is furnished by the redness of the skin which rapidly follows a simple scratch or cut, and which then vanishes in a short time. The stimuli travelling by the roundabout way, through the vaso-motor centres of the cord, are generally weak, and only stimulate the peripheral inhibitory centres *g*. They play an important part in the spread of nervous and parasitic dermatoses : in the latter case by producing a hyperæmia which makes the skin a more favorable soil. Constriction of all the arteries of the skin, by cutaneous stimuli travelling along the indirect path, occurs, as we have already seen in anæmia, only if the stimuli are very violent. Universal cutaneous anæmia is the precursor of cerebral anæmia (fainting), which generally soon follows. There are only the two sets of fibres, *h*—*m* and *h*—*g*, for the action of sensory nerves on the cutaneous circulation.

Ludwig and Cyon[1] found that the stimulation of a certain cardiac nerve in the rabbit caused all the cutaneous arteries to dilate. Considering the abundant supply of regulative machinery for the peripheral vessels, it would have been surprising if no means had existed for the direct interference of the centre itself of the vascular system, viz. the heart, in the action of the vessels of the skin. In the depressor nerve of the rabbit this means has been found. When the blood-pressure rises, the heart relieves itself by more vigorous and slower beats (vagus stimulation), as well as by paresis of the peripheral vessels. The path *c*—*m* in the diagram is open for this process.

[1] 'Sitzb. d. Sächs Akad. d. Wissensch.,' 1866.

We have, finally, to consider stimuli travelling from the cerebrum to the vaso-motor centres (*p*—*g* in the diagram). These explain the influence of psychical emotions on the cutaneous circulation. As is well known, the unstriped muscle of the cutaneous vessels is as little under the influence of our will as any other tissue of the kind; our conscious thinking has not the slightest effect upon it. But certain conceptions, especially those causing shame or anger, can also, when they cross the threshold of consciousness, unconsciously affect in such a manner the vaso-motor centres that the arteries of the skin in certain regions are paralysed for the time. The stimuli passing down the path *p*—*m*—*g* are generally only strong enough to stimulate the peripheral inhibitory centres, and these too not even universally, since the blush for the most part only pervades the skin in the region of the head. Thus the effect produced differs from the above considered universal pallor caused by psychical disturbance (by the path *p*—*m*—*d*). Now, looking back at our diagram, we see that the path *m*—*g* is the most important; it is, so to speak, the most active of all. In *m* a number of internal and external stimuli continually run together, to be conducted to the arterial tube, increased in number by the arterial stimuli originating independently in *m*. Instead of allowing antagonistic sets of muscular apparatus to counteract one another in the wall of the artery itself, by there being a second similar nervous mechanism with its subordinate muscles, there is the simple arrangement that all the stimuli for the arteries, which unchecked would lead to constriction, must pass through peripheral ganglia, in which they can be wholly or partially inhibited, according to the requirements of the individual arteries. As a single workman can hold in check the whole latent water-power behind a flood-gate, so very weak stimuli affecting this particular spot suffice to keep all those tonic influences away from the artery and to paralyse it. Hence it is chiefly with paralysing or inhibiting influences that we have to deal in the chapter on hyperæmia. The peculiarity of the cutaneous vessels is their powerful tonic contraction (in contrast, *e. g.* with the vessels of the lungs). Hyperæmias, or at any rate the so-called arterial ones, are hence, without exception, para-

lytic phenomena; and we see how inappropriate, and even misleading, is the expression "active hyperæmia," which is so often used. The "hyperæmias of stagnation" might be much more appropriately termed "active," for here the tone of the vessels comes much more into consideration than their name indicates. It would, indeed, be better to avoid altogether the misleading terms "active" and "passive." If we do not wish to speak of "paralytic" hyperæmias, we might very well employ the words "relaxing" or "fluctionary," which also contrast well with the expression hyperæmia of "obstruction." Clinically, then, two classes of hyperæmias are known by the bright red colour of the former, and the bluish-red (cyanotic) tint of the latter; anatomically they are distinguished by the accelerated blood-stream in the former and the retarded in the latter. The terms "hyperæmia of relaxation" and "hyperæmia of obstruction" hence cover the most important external characters.

## III. Relaxive Hyperæmia.[1]

Cohnheim has taught us that the best cure for all injuries to the vessels is an increased flow of blood through them. An increased supply of blood to the vessels is only possible by a removal of the normal obstructions to the circulation; and this, especially for the arteries of the skin, means a diminution of their tone. The capillary area of the skin, especially the papillæ, is immediately exposed to the full force of the blood-pressure, which is usually broken in the arteries. The skin becomes red, gets hotter, and gives off more heat. While no pathologist would look upon the pustules of smallpox as the result of a toxic angioneurosis, such a view of the nature of a prodromal exanthem is, at least, plausible. The former condition is a type of an infective embolism of the skin; the latter is the result of the action of the poison on the central vaso-motor system.

[1] "Wallungshyperämie," 'Monatsh. f. prakt. Derm.,' Bd. ix, 1889, No. 6. [I have been unable to find an accurate and altogether satisfactory translation for this expression, which literally means a "welling up."—Ed.]

The prodromal exanthem seldom affects the whole body; it has a predilection for the flanks and for the flexor surfaces of the arms and legs. Hebra showed that the later eruption does not affect these regions, and he tried to prove a connection between these two facts. The author agrees with Curschmann that no such connection exists. The above-mentioned regions are generally free from the eruption of smallpox, even when no prodromal rash has appeared; and we know that in leprosy these same districts are usually unaffected, although no previous hyperæmia of them has taken place.

In contradistinction to this is the roseola which appears in the convalescent stage of cholera. In this case the acute intoxication of the body is over; the blood once more circulates through the contracted arteries and capillaries, and causes, where the stasis was most marked, at the tips of the extremities, a red, patchy (less often an urticarial) exanthem. There is here no question of embolism or of poisoning of the vaso-motor centres, but only of a flooding of the most contracted, and probably the most injured vessels with blood. The general contraction of the vessels in the algid stage, as in the resolution of Reynaud's disease, probably accounts for the fact that these paralysed vessels show no symptoms of inflammation. To understand the occurrence of this roseola we must study the arrangement of the vessels of the skin.

The arteries and corresponding veins of the skin, from the time they enter the hypodermic tissues, form cones, the apices of which lie in the subcutaneous tissues, the bases in the papillary bodies. According to the fibrous nature and thickness of the cutis, the axes of these cones lie either vertically, or more usually obliquely, to the surface of the skin. These cones are cut by the under surface of the epidermis into rounded or elliptical conic sections, and as a result the papillæ are composed of round or oval portions of greater or less diameter. Even when the skin is well supplied with blood these vascular cones can only touch each other at various points, and lacunæ are left between them.

In most parts of the body, especially in the extremities,

the vascular cones are bounded by or embedded in a large mesh-work of capillaries, which have no direct supply and return of blood.

We can easily see that there are many disturbances of the circulation which must cause such an unequal distribution of blood as to produce differences of colour. The roseola of cholera arises when, after prolonged stasis in the capillary area, the blood presses forward into this district: the stasis here is not so quickly overcome as that in the papillary areas.

Characteristic of simple vaso-motor disturbances is the erythematous circular syphilide which arises in the later secondary stages. It is distinguished from all circular serpiginous eruptions of the same period by the fact that the circles do not enlarge, that they have no sharp external edge, and that their centres are usually quite healthy. It is, in fact, not a syphiloma of the skin itself, but of the nerves of the vessels. The circles themselves correspond to the collateral capillary network, their centres to the papillary vascular elements. Similar erythemata arise in *lepra nervorum;* besides sharply defined erythemata, spots and circles appear, which later form circular or gyrate patches, that in time become pigmented.

A whole series of toxic erythemata is allied to these indirectly infective eruptions. The first group comprises the erythemata caused by atropine, amyl nitrite, and chloral. These are transient, diffuse, and are like a blush called forth by shame or anger, especially as they affect the head and neck.

Atropine erythema affects the upper part of the trunk; chloral rashes the wrists, ankles, elbows, and knees. No desquamation takes place, and no subjective symptoms accompany them; they are merely paralytic phenomena.

A draught of cold water calls forth an enormous hyperæmia of the head in patients who habitually take chloral.

Here we have a latent weakening of arterial tone, which is only manifested by additional influences—a good example of a slight chronic angioneurosis of the skin. We may regard quinine erythema as a prototype of a second group. This rash is more universal, of longer duration, it causes desquamation and œdema, is accompanied by subjective

sensations and by fever, and is liable to be confounded with scarlatina. The internal administration of salicylic acid, carbolic acid, stramonium, veratrine, and digitalis causes general hyperæmia of the skin. And these rashes are not brought about by a vaso-neurosis alone; the toxic material injures the vessel walls, and thereby causes the symptoms of a slight cutaneous inflammation.

A third group is represented by the antipyrin rash; this drug gives rise to discrete, raised, somewhat œdematous, itching papules, which are not unlike the rash of measles. It affects chiefly the neighbourhood of joints, seldom the trunk, and less seldom the face, neck, and genital organs. The subjective symptoms are more pronounced, desquamation less so, than in the erythemata of the second group.

To this group belong the morphia, cubebs, and copaiba rashes, and those resulting from the administration of turpentine, hyoscyamus, and chlorate of potash.

We now turn to the relaxive hyperæmias that have a more local character, and we may divide them into three groups.

1. The first group includes those erythemata in which the paresis of the muscular coat of the arteries is called forth by physical causes. We must mention first of all the hyperæmia which results from the cessation of any pressure upon the skin, such as is seen after the application of an Esmarch's bandage, or in the red lines left on the skin by drawing one's finger-nail across it.

The author looks upon this as a pressure paralysis of the individual capillaries and arterioles—as an idio-paresis, and not a paresis brought about by the intervention of the vaso-motor centres.

2. Hyperæmia caused by variations in temperature is seen in newly born children. Cold has a paralysing effect upon the vessels only when they have been exposed to its influence for some time. The reactionary paralysis brought about by low temperatures lasts only as long as the application of the cold continues.

3. The paralysis of the vessels caused by heat must be differently explained. Warming the skin does not directly paralyse the vessels; it causes a more rapid and consequently

warmer flow of blood through them, and so indirectly causes a paresis of the muscular coat.

At a temperature of 50° to 60° the hyperæmia gives place to slight degrees of inflammation.

We have here an irritant which, according to the extent of its action, causes either muscular paresis or injury to the vessel walls.

To this class of irritants the rubefacients belong, as do also the mineral acids, iodine, mercury, &c.

We may class the erythemata caused by inoculation of poisonous substances given off by insects (bees, wasps, &c.) in this group. The ætiology of the infective hyperæmias is still doubtful. They show no relations to the anatomical arrangements of the cutaneous blood-vessels. The closer we examine these exanthemata (scarlet fever, measles, typhoid rash), the more we are convinced that each of them has characteristics of its own, dependent upon a particular infective germ.

## IV. Obstructive Hyperæmia.[1]

The author has defined "relaxive hyperæmia" as a congested condition of the skin, in which the resistance in the peripheral vessels is abnormally small while the blood-current is quickened. By "obstructive hyperæmia" he understands a condition of increased vascularity, in which the resistance is abnormally increased while the blood-current is slowed.

The increase of resistance which causes congestion may occur at any point in the circulation, in the right or left heart, in the arteries or veins.

Congestive hyperæmia of the skin is, however, more simple, and he divides it into two classes according to the general or local character of the congestion.

A dark bluish colour and an objective, sometimes subjective, lowering of temperature, are characteristic of all

[1] "Stauungshyperämie," 'Monatsh. f. prakt. Derm.,' Bd. ix, 1899, No. 8.

congestive hyperæmias, and œdema of the tissues often occurs. The functions of the skin are mostly suspended, though an increased secretion of sweat is common enough. Hypertrophy of the tissues does not occur even in long-standing congestion; more often pressure atrophy and increased vulnerability are noticed.

After discussing the causes of cyanosis, the author points out that we cannot explain the bluish fingers, ears, and noses of patients with weak hearts on the ground of the distance of these parts from the heart. He thinks that the vessels of these parts contract under the influences of decreased pressure and external temperature, because they are from their position normally exposed to greater losses of heat. He looks upon the contraction as a compensatory phenomenon.

The author then describes the occurrence of congestive hyperæmia as a result of pressure on large vein trunks by tumours, the pregnant uterus, &c.

Besides an inflammatory acne rosacea, he describes another non-inflammatory form. In both forms obstructive hyperæmia plays an active part; isolated, large, dilated veins appear about the *alæ nasi*, the tip of the nose, and on the cheeks; later a network of dilated capillaries arises, giving a diffused redness to the organ. The obstruction to the circulation in the inflammatory form (rosacea seborrhoica) may lie in the inflammatory process in the skin; in the non-inflammatory form the congestion may be caused by obstructions to the circulation in the nasal mucous membrane or about the fauces.

Auspitz first pointed out that circumscribed bright red patches appear on the congested, bluish-grey surface of an arm round which a ligature has been placed. Besides these red patches, in cases of extreme congestion white patches appear. The author agrees with Auspitz that these white patches are due to anæmia, and he thinks that they are caused by contractions of some of the arteries supplying the skin.

Auspitz considers that the red colour of the above-mentioned patches depends upon the presence of hæmoglobin in the exudation. The colour changes from a

yellowish to a fiery red, and it disappears when the congestion is relieved, leaving brown pigmented patches.

Cold is an important factor in the causation of obstructive hyperæmia; it not only causes contractions of the arteries and veins of the skin, but it also acts upon the vessel walls, indirectly by slowing, and eventually cutting off the blood supply. It also cuts off the supply of oxygen to the muscular coat of the vessels. The vessels contract until their lumen almost disappears, by which the antagonistic nerve apparatus of the vessel walls is stimulated, and the anæmia is transformed into a relaxive hyperæmia. Under greater degrees of cold, however, this antagonistic nerve mechanism is interrupted, and the skin turns suddenly white and becomes like a piece of frozen snow. This is well seen when the skin is frozen with ether spray. The veins of the skin have a muscular coat as well as the arteries, and this coat when acted upon by cold contracts, and so gives rise to an obstruction in the circulation which causes congestive hyperæmia.

When the arteries and veins contract equally the flow and return of the blood are proportional; but when the return of the blood is in any way hindered, peculiar appearances arise.

Chilblains have nothing to do with frostbite; they are "angioneuroses," and depend upon a perverse reaction of the vessel tonus to differences in temperature.

The arteries of the affected parts contract somewhat under the influence of cold, the veins contract more strongly, and the result is a slowing of the blood-current, which is evidenced by a bluish colour and slight swelling of the parts. No paresis of the arteries, which would lead to a compensatory relaxive hyperæmia, takes place. The supply of blood to the parts is not large enough, and the obstruction to the return of the blood is too great.

Dry cupping causes an obstructive, and not a relaxive hyperæmia of the skin. It leads, if the cup is left on the skin long enough, to complete stagnation and diapedesis of red corpuscles.

The force of gravity may cause a congestive hyperæmia, as is well seen in the well-known blue death-marks on dependent parts of the body. During the death-agony a

general contraction of the arteries drives the blood into the veins; when the rigor mortis ceases the blood from these regurgitates into the capillary areas, which become enlarged and of a bluish-black colour.

The author then describes the congestion of the legs and feet which occurs in people who stand a great deal; and he traces the steps by which the veins, from being merely over-filled in the earlier stages, become varicose later on.

## V. Œdema.[1]

We must distinguish between two kinds of œdema, inflammatory and mechanical.

The pathology of MECHANICAL ŒDEMA of the skin has not been sufficiently studied, and is generally misunderstood. Experimental pathology has taught us that the closure of all the lymphatic channels of a limb does not cause œdema in it, while an obstruction in the veins never fails to give rise to œdema.

As a natural conclusion from these two facts, the author states that the lymphatics of the skin are only an occasional channel for the return of lymph. The lymphatics of the skin carry back to the blood only that small fraction of lymph which does not return by the venous capillaries into the veins.

The skin is able, by means of its permanent elasticity, to drive along the lymphatics the small quantities of lymph which they normally contain. A more extensive employment of the lymphatic channels is abnormal, and leads to a softening of the tissues,—to, in fact, œdema. We do not, of course, deny that obstructions in the lymphatics themselves, especially when they are numerous and high up, may increase œdema. The discovery of such obstructions, however, even the complete obliteration of the thoracic duct, does not by itself explain the occurrence of œdema of the skin.

In every case of œdema we have to determine what has prevented the lymph of the skin from returning by its proper channels, the veins.

[1] "Oedem," 'Monatsh. f. prakt. Derm.,' Bd. x, 1890, Nos. 3 and 4.

The amount of œdema depends not so much upon the intensity of the obstruction in particular vein-trunks as upon whether all, or at any rate most of the veins of a region are pressed upon.

1. The most certain way to produce œdema quickly is to compress the upper part of a limb with a bandage. The veins are more easily compressed than the arteries, and the return of blood is thereby impeded, while the amount of supply is not decreased. In this case compression of the lymphatics takes no part in the production of the œdema.

2. The second chief factor in the production of mechanical œdema is gravity.

3. General venous congestion causes œdema of the whole skin, which shows itself first in particular places—ankles, eyelids—depending on the structure of the skin in these localities. The œdema of heart disease is of mechanical origin; no changes in the vessels of the œdematous skin occur.

4. Venous thrombosis.—This generally takes place in the smaller veins, such as the crural; the amount of the consequent œdema depending, first, upon the number of available collateral branches; and secondly, upon the presence of other causes of œdema, such as inflammatory complications, general hydræmia, &c. In otherwise healthy people, thrombosis of the crural vein causes only slight œdema about the ankles and feet.

*Phlegmasia alba dolens*, and inflammatory conditions of the skin leading to elephantiasis, were usually looked upon as a lymphangitis with retardation of the flow of lymph. We now know, however, that obstructions to the lymph-stream never cause œdema of the skin. In *phlegmasia alba dolens* the fact of the lymph being richer in albumen shows that we have to do with an inflammatory process, which, starting in an infective phlebitis, spreads to the surrounding tissues. We can speak of it as an inflammatory œdema—a combination of inflammation and stagnation.

In *elephantiasis filariosa*, and the lymphorrhœa connected with it, great weight has been always laid on the plugging of the lymphatics by filariæ, although the presence of the embryos in the blood-vessels has long been known. It is in

the veins, and not in the lymphatics, that we must search for the obstructions to the lymph-stream, even when plugging of the lymphatics can be demonstrated.

5. Among the mechanical œdemas the author places the collateral œdema which is often noticed above some deeper seated abscess, as on the the cheek in empyema of the antrum, &c. The œdematous skin is not hot or red, and the œdema disappears when the abscess is opened.

Cohnheim, Rindfleisch, and Ziegler look upon these serous swellings as inflammatory. Zimmermann pointed out that this œdema occurs over the sternum or ribs in cases of pleuritic effusion, which, he says, disproves its inflammatory origin, as does also the fact of its rapid disappearance after abscesses are opened. Billroth and v. Recklinghausen look upon this collateral œdema as brought about by a stagnation which might easily be caused by compression of neighbouring veins.

The author thinks that this œdema is a mechanical one; and if the fluid from the œdematous tissues contains little albumen and few white corpuscles, he looks upon the stagnation theory as justified. We know, he points out, that veins coming from inflamed tissues are dilated: stagnation of blood in the tissues surrounding the focus of inflammation must, therefore, easily occur; and if a relaxive hyperæmia spread into this same area, an obstruction œdema will result.

6. Contractions of the walls of the veins as a cause of stagnation of the blood.

The author has pointed out that this factor has been entirely overlooked in the study of œdema; and he says we only need recognise it in order to understand the spastic œdemas of the skin—urticaria, and the circumscribed œdema of Quincke.

This theory, based on the *tonus* of the walls of the veins, explains the origin of urticarial skin diseases.

The author found, in every case of urticaria on the arms or legs, that if a bandage were tied round the limb as soon as the general venous congestion set in, the urticarial swellings became flattened and depressed, and itching ceased. Indeed, at some distance from the ligature one can easily see that the urticaria disappears before a general

swelling of the skin is noticeable. These facts agree very well with the theory according to which the urticarial swellings are caused by a local obstruction to the return of the blood. The increased pressure in the larger veins of the skin (caused by the ligature) overcomes the spasm of the smaller veins. By spasm of the veins he understands a sudden contraction of the musculature of these vessels, which may last a variable time, and disappear quickly or slowly. This contraction must always be greater than the corresponding contraction of the arteries; and the disproportion between the arterial and venous tone is the chief factor in the occurrence of spastic œdema.

We must include in this group the œdema of erythema multiforme, and the so-called rheumatic and neuralgic œdemas.

Œdema occurring in paraplegic and paralysed people must be differently explained. When, in these cases, the vaso-motor nerves of the limb are paralysed, the peripheral vaso-motor centres take over the regulation of the calibre of the vessels; hyperæmia gives place to anæmia; and, if the tonus of the veins preponderates, œdema occurs.

To this group of nervous œdemas, which have all a more or less local character, the author adds the toxic œdemas. These have all the common property of causing, by some material circulating in the blood, a disproportion between the tone of the arteries and veins. This is seen in morphia poisoning, in curari poisoning in frogs, and in the œdema occurring before death from snake-bites. Until a more plausible explanation be forthcoming, there may be added to this group the œdema occurring in renal disease and scarlet fever.

The so-called climatic dropsies which occur, sometimes epidemically, in hot climates may be regarded as of a toxic nature, and something akin to "*urticaria ab ingestio.*"

Circumscribed, slight, transient œdema (without albuminuria) is sometimes noticed in people living in the tropics; this may be caused by an inco-ordination in the tone of the arteries and veins. This increased tone of the vessels is antagonistic to the relaxing effect of the heat; an increased arterial tone would give rise to anæmia, and increased venous on e to œdema.

The author thinks that the œdema seen about the ankles in cases of cachexia and phthisis is due to an auto-intoxication which affects the vaso-motor system.

Inflammatory Œdema.—We can only speak of inflammatory œdema when actual acute, subacute, or chronic inflammation exists.

Whenever the skin is inflamed, it becomes swollen, because the power of absorption of the veins is small, and the increased amount of lymph has to be carried off by the lymphatics. Inflammation of the skin, therefore, more than of other organs, causes abnormal conditions of circulation of the lymph, and more readily induces swelling. Inflammatory œdema of the skin occurs chiefly in acute inflammations, especially in those brought about artificially by drugs, *e. g.* vesicants, tar, resorcin, &c.

Cohnheim and Lichtheim, and later Jankowsky, showed that if in hydræmic animals the skin were inflamed it became also œdematous. Our experience teaches us that this does not occur in man. Inflammatory skin diseases in wasted, badly nourished, anæmic people tend to decrease to a minimum or disappear, and to show themselves again when the circulation and condition of the blood have been improved.

This important difference is explained by the fact that in the experiments on animals an hydræmic plethora was present, while in the other cases there is merely a diminution in the solid constituents of the blood.

Œdema, whatever its cause may be, represents the difference in amount between the arterial and venous blood; and this definition applies to the inflammatory as well as to the mechanical variety. We thus admit that the fluid of œdema and the physiological lymph are the same; but we only speak of œdema when the above-mentioned difference is very large.

Every œdema which lasts any time, whether it has arisen suddenly (rheumatic œdema) or slowly (renal œdema), causes a gradual loosening of the tissues, and the normal elasticity of the skin becomes lost. The tissues pit when pressed upon, and one can judge of the loss of elasticity in the skin by the length of time that such pitting lasts.

If, on the other hand, a sudden obstruction to the venous circulation arises (as in urticaria, where abnormal nervous impulses raise the tone of the veins), a tense elastic swelling results, which is sharply defined from the surrounding tissues, because the normal lymph-spaces only allow a small amount of the fluid to be carried off.

In cases of extreme œdema, when the cutis is thin, blebs form in the epithelium, which burst, and allow of a constant trickling of lymph (lymph scrotum). The pressure of the fluid may cause necrosis in cases when the skin is greatly thickened.

The secretory functions of the skin in all mechanical œdemas are suspended. The surface is dry, fatless, dull, and often slightly desquamating.

In the simple œdema of heart and renal disease, only symptoms of pressure atrophy show themselves. The skin becomes thinner, the elastic and muscular tissues atrophy, fat disappears, and the veins and lymphatics become dilated.

From this the author thinks that the well-known hyperplastic processes in *elephantiasis nostras* and *filariosa*, as well as in long-standing, artificial, inflammatory œdemas, are not consequences of the œdema, but of the preceding inflammatory changes (erysipelas, eczema, *dermatitis artificialis*).

In the course of these the skin swells enormously; the collagenous network grows to a great size; the epidermis of the skin and follicles forms deep depressions and warty outgrowths; the blood-vessels and lymphatics become not only thickened, but, as their twisting shows, also elongated; the hyperplastic process extends to the swollen glands. These changes are ascribed to an infective cause; simple mechanical œdema, like venous congestion, is associated with retrogressive changes in the tissues.

## VI. Hæmorrhage.[1]

Hæmorrhage in the skin may occur *per rhexis* or *per diapedesis*, being blood effusion in the one case, and blood

[1] "Blutung," 'Monatsh. f. prakt. Derm.,' x Bd., 1890, Nos. 6 and 7.

filtration in the other. Although neither the causes, symptoms, concomitant circumstances, nor final results are the same, we cannot in every case say whether a given hæmorrhage has resulted from rupture or from filtration, and to avoid repetition they may be both considered together, under the common term hæmorrhage. It is, moreover, obvious that the chief causes of diapedesis may act as assisting causes of rupture of blood-vessels and *vice versâ*. It is, however, important to accentuate the marked differences of the two processes. We can more easily decide, in the case of the skin, whether rupture of a vessel has occurred; and imbedded, as the latter is, in a firm, tough tissue, hæmorrhage from it must always be more difficult, and when it occurs, more easily ascribed to either process than in the case of the vessels of internal organs. When rupture takes place, red blood is poured out through a wound of the vascular wall; but when the hæmorrhage is due to diapedesis, lymph passes through, poor in albumin, fibrin factors, and white corpuscles, but abnormally rich in red discs. In the former case a blood pool rapidly forms in the tissue, its size being determined by the surrounding resistance, and this pool is soon converted into a thrombus; but in the latter case the hæmorrhage increases slowly, and its elements are diffused through the neighbouring tissue without becoming a continuous clot. If the hæmorrhages are small, these differences may not be detected by the microscope, especially when the specimens have been hardened.

Hæmorrhages due to rupture may give rise, if small, to "ecchymoses," and if large, to "blood-boils" or "hæmatomata." The cause is nearly always some gross traumatic lesion. The flea-bite is an example of the former, and large and more permanent blood suffusions may be produced by blunt force over large areas, without penetration; the result in this case depending more on the actual vascularity of the skin at the time. Hence, all factors producing stagnation hyperæmia increase the liability to hæmorrhage from rupture. One kind of blood-boil is the ot-hæmatoma of lunatics; but the cephalo-hæmatoma of infants and hæmatomata of the vulva in parturition do not belong solely to this class, for there is at first a stagnation œdema leading to diape-

desis, and these forms show how difficult it is sometimes to draw the line between the two processes. By cupping, the hyperæmia of stagnation may pass into rupture of the abnormally distended capillaries; but the diminution of pressure up a high mountain or in a balloon is not sufficient to cause hæmorrhage in the skin, although it may from mucous membranes, often, no doubt, from the bursting of the inelastic and superficially dried surface covering. A similar result has been attributed to increased pressure within the vessels, but wrongly so in the case of the skin, for the great muscularity of the cutaneous arteries is able to resist the most powerful cardiac action. The case is different if there be great general venous congestion, as during the paroxysms of whooping-cough, epileptic and asthenatic fits, parturition, &c., when small cutaneous vessels may occasionally burst. They are insignificant, however, as compared with those occurring under similar conditions in the conjunctiva, retina, and brain.

Squeezing and suction are, therefore, the most important and certain causes of rupture of the well-protected cutaneous vessels. The causes of rhexis, indeed, are mainly traumatic.

Formerly, too much importance was attached to changes in the vascular walls. Although atheroma and thinning of the wall are doubtless important factors in the case of other organs, the small cutaneous arteries are far more subject to the opposite conditions—endarteritis obliterans and thickening of their walls. The theory of fatty degeneration of the cutaneous vascular endothelium must be received with caution, for the fat globules deposited by the lymph are by no means a sign of a degenerative process.

Two kinds of vascular changes, however, remain, which may predispose to hæmorrhage:—(i) Atrophy of the venous walls from pressure, as we see now and then in old varices, and (ii) an imperfect embryonic nature of the cutaneous vessels. The first causes not only profuse hæmorrhages, but also circumscribed ecchymoses in old people, whose skin is already atrophic. Arrested vascular development often gives rise to hæmorrhage from tumours, especially the sarcomata; but here there is also considerable dilatation of

the larger blood-vessels. It seems probable that some of the hæmorrhages of newly-born syphilitic infants are also due to imperfect development of cutaneous vessels, but true (embolic) purpura also occurs. The so-called cachectic hæmorrhages, however, must not necessarily be attributed to atrophic or degenerative vascular changes. They chiefly belong to processes of diapedesis; a cutaneous hæmorrhage in a cachectic individual is hardly ever due to cachexia of the vessels.

An affection of the general vascular system may be mentioned, which alone deserves the name of a hæmorrhagic diathesis, viz. hæmophilia, in which Schönlein and others found a thinness of the vascular walls. The condition is hereditary, and the male members of the family, with thin, little pigmented skin and fair hair, are chiefly affected. Spontaneous hæmorrhages in the skin, without laceration of the cutis may occur; and the slightest mechanical injury may entail serious hæmorrhages and hæmatomata. As there is no want of coagulating power in the blood, the difficulty of stopping the bleeding from insignificant wounds can only be the result of deficient retraction and elasticity of the arterioles. But here trauma is also the important exciting cause.

In proceeding to the cutaneous hæmorrhages resulting from diapedesis, we enter the wide and dark field of purpuric diseases. Only in those occurring in simple venous congestion, have we a satisfactory experimental basis in the observations of Stricker, Cohnheim, Auspitz, &c. But these are of less interest to us than those occurring in connection with infective processes and neurotic disturbances. They have been generally classed as "mechanical," in distinction to those forms of purpura supposed to be dyscrasic and toxic, and due to a change in the blood rather than of the conditions of the circulation. This idea, however, on careful investigation, is untenable, for we may also give a "mechanical" explanation to the toxic and infective forms. It is hence necessary to give the so-called mechanical forms of purpura another name. They mostly result from "simple congestion" (stagnation); and they are the simplest forms of cutaneous hæmorrhage from diapedesis. Their prototypes from experimental pathology are the petechiæ, which we can

produce at will below a venesection bandage; and Auspitz first showed us, by his stagnation experiments, that venous congestion alone suffices to produce macroscopic hæmorrhages, even in healthy skin. The congestion must border on stasis, but in certain diseased conditions lesser degrees of congestion suffice. In scarlatina and erysipelas a purpuric eruption is easier induced than with the normal skin; and still more so in a acute dermatitis, acute eczema, urticaria, and measles. Cutaneous hæmorrhage is enormously increased by simple congestion in the case of purpura variolosa, the whole limb showing a suffused black colour. In one category of cases under this group the stasis of blood in the larger veins is the sole cause of the hæmorrhage, as in the rare petechiæ after thrombosis, *e. g.* in phlegmasia alba dolens. Extravasations in varicose legs, although belonging to the same class, are not so easy to explain. Varices are not due simply to gravity, but to a chronic gravitation-hyperæmia in connection with an increased tone of certain vessels of the limb, and consequent diminution of the *vis a tergo*. Extravasation is the result, especially where the skin is atrophic, as in the neighbourhood of chronic ulcers. The preagonal purpura, developed on dependent parts shortly before death, is related to this. It originates from the general venous congestion and gravitation-hyperæmia caused by deficient *vis a tergo*, and is an example of so-called "cachectic" purpura. Here, too, spasm of the small cutaneous veins so resists the pressure in the venous capillaries, that diapedesis of red disks can take place. This is also the case in very chronic urticaria, urticaria perstans (Pick), erythema multiforme of the legs, purpura urticans, and in lichen lividus of old people. Bateman's purpura senilis may be here mentioned, which occurs chiefly on the extensor surface of the forearm in old women, and is very chronic and accompanied by dark pigmentation.

The larger group of infective and toxic pelioses were formerly explained by "blood-dissolution," the poison being supposed to produce so profound a change in the blood that it passed easily through the wall of the vessels, as in purpura variolosa and severe yellow fever. This idea is erroneous: before such a diapedesis of red discs, considerable œdema

would first be seen, and we should also have to assume severe lesions of the vascular walls, or a common inflammatory exudation. It has been abundantly proved experimentally that heterogenous substances, so long as they do not cause coagulation, may be added to the blood without hæmorrhage resulting.

Medical practitioners mean by the term a peculiar unknown lesion of the vessels leading to the diapedesis; but inflammatory changes in the skin occur only exceptionally in the various forms of purpura, *e. g.* in *P. urticans;* and diapedesis from circulating blood, without previous and concomitant exudation of inflammatory lymph, cannot be accepted. The case is different, however, if simple congestion or stasis is present. Hæmorrhagic inflammations, indeed, are to be regarded as composed of inflammation *plus* stasis, the cause of the latter being unknown. Inflammation without stagnation cannot give rise to the diapedesis of red disks.

Hayem has recently supposed the coagulation of blood by "précipitation grumeleuse" the cause of these "dyscrasic" hæmorrhages. He found that ox serum introduced into a dog's circulation produced hæmorrhage in the intestine, serous membranes, spleen, &c., and that these were often embolic, the capillaries being plugged by changed hæmatoblasts; but they were not observed in the skin, hence, if the explanation be even correct, it is not applicable to human purpura. Simple emboli produced by chemical blood changes are not sufficient to explain suffusions, &c., in the skin. Here there are no terminal arteries; and the permanent plugging of even small vascular areas would require very numerous emboli. In general embolism, moreover, hæmorrhages are observed much more frequently in internal organs than in the skin.

Nor can cutaneous hæmorrhages be accounted for by isolated venous thrombi, which are difficult to distingnish histologically from columns of stagnating blood. The collateral circulation is too good for thrombosis to cause hæmorrhage or œdema in the skin. The thrombus, moreover, may be a consequence of the same changes in the capillaries which cause the hæmorrhages. V. Kogerer found venous thrombi in thirteen cases examined by him, but they alone are not

enough to explain the petechiæ. It is more likely that the fibrinous clots, also found by him, in the capillaries and arteries were the primary cause. The continuous blocking of whole capillary areas, due partly to changes in the vascular walls and partly to a continuous formation of thrombi, goes much further towards explaining the infective cutaneous hæmorrhages.

Amyloid capillary degeneration, with cutaneous hæmorrhage, was found by Wilson Fox in a case of syphilis; but this is exceptional. Hyaline degeneration is often found in chronic dermatoses, but never amyloid. Askoro described considerable endothelial thickening in specimens from a scorbutic gum; and Leloir observed a peculiar proliferation of endothelium, and its partial detachment in cutaneous hæmorrhages, which occurred shortly before death in a case of cirrhosis of the liver with interstitial nephritis and atheroma of the aorta. The vessels were dilated, especially in the papillæ, and there was vigorous emigration of leucocytes; but no fibrin plugs were formed. He attributed the obliteration of the capillaries, partly to a stagnation of white discs, and partly to the desquamating endothelium. Hayem has similarly attributed cutaneous hæmorrhages, in a case of phthisis and peliosis rheumatica, to endarteritis obliterans. It is not likely, however, that this process, which occurs so commonly in the skin without producing anything of the kind, should by itself cause hæmorrhage. Endophlebitis obliterans, on the other hand, might cause stagnation diapedesis, &c., but it is not known to occur. The plugging of the arteries with finely granular matter, also observed by Hayem, is of more importance. Endarteritis can only assist by lowering the pressure and velocity of the blood-stream.

In purpura hæmorrhagica Letzreich found bacilli and spores imbedded in gelatinous plugs, produced, he thought, by the action of the organisms on the serum albumin, and completely filling the capillaries. It is likely that in Hayem's cases, and in many other forms of purpura, a similar process of bacterial emboli is in question, with clotting of plasma along extensive tracts, consecutive stagnation and diapedesis.

Klebs was the first to connect cutaneous hæmorrhages with bacteria. He found colonies of his "monas hæmorrhagi-

cum" blocking the vessels and causing hæmorrhage in a form of purpura of new-born infants. Diarrhœa ushered in the disease, and a parasite in the intestine was probably primarily concerned. In his steps followed Cornil, Martin de Geniard, Coppinger, Petrone, Cohnheim, and Weigert. The infective forms of purpura are most simply explained in this way; and the theory of bacterial coagulation thrombi will probably in future play an important rôle.

That thrombi may form around other bodies than micro-organisms is not to be denied; but we cannot believe in spontaneous coagulations as a cause of hæmorrhage in the skin.

Harris has observed cutaneous hæmorrhages in three cases of lympho-sarcoma of the mediastinum, and in some of the specimens there were sarcomatous plugs in the capillaries. A connection between sarcomatous growths and hæmorrhage in the skin has also been maintained by Fagge.

In the present state of our knowledge, we must accept the following ætiologically different forms of purpura:

(1) The simple pelioses due to congestion (stagnation). These are not so common as is generally assumed, for the venous congestion is often accompanied by other causes of purpura.

(2) The acute hæmorrhages occurring in infective diseases. The notion of "blood-dissolution" is obsolete, and Hayem's theory of coagulation of granular precipitation must yield to the view of mixed fibrino-bacterial or hyalo-bacterial thrombi.

(3) Those rarer cases due to obliteration of capillaries from leucocytes, sarcomatous masses, &c., and in which thrombosis from fibrin formation may subsequently take place.

(4) Those following widely spread degeneration of capillaries (capillaritic desquamation and amyloid degeneration). The changes in the larger vessels of endarteritis obliterans can only, like venous congestion, promote the capillary thrombosis.

(5) The hypothetical toxic purpura, occurring in acute poisoning and in certain chronic diseases. Hayem's theory of spontaneous coagulation around hæmatoblasts is more likely to be true in these cases.

The nervous hæmorrhages of French observers. Strauss petechiæ in tabetics, over painful spots, and Faisans them in neuralgia. Many hæmorrhages in cancer cords of the spine may, perhaps, be here included, as the angio-neuroses, urticaria, and erythema multi-

It is conceivable that a venous spasm may be , and that if the congestion be enduring, exudation stasis will result. Accurate clinical and histological ations are here needed.

time to discard the notion of "cachectic purpura" as well as that of "blood-dissolution." When occurring in ill nourished, alcoholic, or old patients, these hæmorrhages probably belong to one of the first three groups; the debilitated action of the heart, and the lowered blood- in the capillaries in such cases, are no doubt favour- the formation of thrombi by bacilli, &c.

## VII. Angio-neuroses.

we must give the credit of having first sepa- skin affections, under the name of "Angio- ," from the ordinary inflammatory having clearly defined this class.

a quotation from Auspitz's work, in which pointed out of forming a distinct class of skin affections." Auspitz considers that the the blood vessels are independent of processes, but are dependent upon injuries the vascular nerve-centres: therefore, the localisation in the skin in each particular the nerve disturbance and the has no very clear ideas as to vessel terms is combined with the necessary that we should clearly the processes in every case the most different combinations of

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these two factors. In a large number of cases we have not to deal with a widely distributed neurosis and a local circumscribed inflammation of the skin, but the angio-neuroses and inflammation occur in the same small vascular areas, and run a parallel course, *e. g.* Hebra's erythema multiforme of the dorsum of the hand. In such a case we must imagine that the specific virus is seated in the skin at these places and calls forth a localised inflammation and an equally circumscribed angio-neurosis.

Such a double action is difficult to imagine, if we merely take into consideration, as Auspitz does, a stimulation or paralysis of the vaso-dilators, or the vaso-constrictors. In no case can we convert a simple inflammatory erythema into an erythema multiforme by stimulating the vaso-constrictors. In a former lecture the author enunciated a theory to account for some special varieties of pure angio-neuroses. Every disproportion in the amount of contraction of the arteries and veins of the skin which limits the amount of blood returning by the veins, causes a spastic œdema of the skin ; and the varieties of urticaria are types of this condition. To this group of angio-neuroses must be added a large number of skin diseases—numerous drug exanthemata, a number of infective erythemata and most of those papular and papulo-bullous dermatoses which are caused reflexly, and lastly some diseases of unknown ætiology, which are akin to E. multiforme and E. nodosum.

When we study these cases more closely, we see that such angio-neuroses can only occur upon erythematous bases ; for simply anæmic angio-neuroses, as in Raynaud's disease, can never lead to insufficiency of the venous blood return.

"In all cases the chief characteristic of an angio-neurosis consists in the fact that the engorgement of the capillaries is not normally compensated for by an adequate fluctuation in the calibre of the veins, and by an increased rate of flow, but that, on the contrary, a stoppage takes place."

The whole process takes place somewhat in this way. At first local hyperæmias occur of the size of macules, or groups of macules in the form of rings, which from their usually symmetrical occurrence point to an irritation of the central ganglia. This first stage cannot be looked

upon with certainty as angio-neurotic; its appearance only suggests it. After a longer or shorter period these spots become, by swelling of the cutis, converted into an E. papulatum. At the same time, the colour changes to a more bluish-red, cyanotic tint. A spastic obstruction to the return of blood has now been added, and the veins can no longer cope with the amount of blood which is brought to them.

The author thinks we may presuppose a special irritability of the musculature of the venous vessels, which reacts in this unsuitable way upon the increased blood-pressure. Most of these cases occur in anæmic, neurasthenic or neuropathic people, in whom muscular spasms of other kinds easily occur. We may suppose that the arteries have the same character of reacting to variations in blood-pressure as we have ascribed to the veins; but the much greater arterial blood-pressure presses upon the paretic arteries, and overcomes any tendency in them to spasm,

The obstruction, which is the characteristic of the angio-neuroses, is caused by a tendency of the whole cutaneous vascular system to reply to a stimulus, such as the increased blood-pressure, by a quick and intense increase in muscular tone.

Our study has now led us to a clear pathological foundation which we may describe as "an intense irritability of the musculature of the cutaneous blood-vessels," which underlies a large number of inflammatory as well as non-inflammatory angio-neuroses.

When the muscular stimulus goes on increasing, a time must come when the muscles of all the cutaneous vessels remain in a condition of tetanic spasm. The clinical picture then changes. There is no incongruity in the calibre of the vessels, as only a very small stream passes along the arteries and veins. This condition is an exact picture of those appearances which have been described as Raynaud's disease and "dead fingers" in the lecture on anæmia. The stimulus of blood-pressure is not sufficient to call forth these appearances; to it must be added the intense cold of the extremities in order that this tetanus of the vessels should be produced.

In some persons a flea-bite only causes an arterial congestive hyperæmia, which does not alter its character when acted upon by new stimuli. In other people the same injury gives rise to an angio-neurotic erythema, because in them the virus is a sufficient stimulus to bring about the irritability of the muscular coats of the vessels.

Various stimuli give rise to angio-neurotic erythemata in different people, such as the weals left on some hands by stroking them with a pencil; *urticaria ab ingestis* and the rashes which occur after the use of certain drugs are of the same nature.

In relation to the cause, an angio-neurosis is the result of a particular or adequate stimulus; in relation to the individual, it is the result of an idiosyncrasy. In the second place a typical, usually rapid, course (synchronous with the cause) is common to all angio-neuroses. As the third symptom common to all angio-neuroses, one must mention their symmetrical distribution.

The character of the eruption is various; papules, vesicles, tubercles, &c. occur, though they are all mostly formed on one type.

The author goes on to discuss the classifications of angio-neuroses as adopted by Auspitz, Lewin, and Schwimmer, and gives a list of eruptions which he thinks should be counted among the infective angio-neuroses;—namely the roseola of cholera, the prodromal rashes of variola, the evanescent erythemata occurring after vaccination, and, perhaps, the roseola seen in tubercular meningitis.

The erythemata, on the other hand, which occur in the course of typhus, typhoid, diphtheria, dysentery, and pneumonia, &c., he looks upon as either embolic or caused reflexly, the latter especially when, instead of simple erythemata, papular or urticarial eruptions arise.

To this latter group he would add, the ephemeral roseola-like rashes which occur in childhood, and which are usually classed under the name *Roseola infantilis*.

The author does not agree with Auspitz in his classification of toxic angio-neuroses. He would class under this heading only the erythematous, erythemato-papular, herpetic, pemphigus-like and urticarial forms.

Auspitz called his third group of angio-neuroses the "essential" one. The word essential means in this connection, as everywhere else, that the etiology of the cases in this group is unknown. It comprises the idiopathic angio-neuroses whose nature is only known to us by the character of the eruptions, and consists of "urticaria chronica" (Cnidosis) and the group of *Erythantheme essentiale*, which, besides Hebra's E. multiforme and nodosum, contains a number of herpetic and pemphigus-like eruptions, and finally Peliosis rheumatica.

Auspitz in his system advocated that the terms E. multiforme and nodosum should be given up; the author does not agree with this, but urges that they should be more accurately defined.

Hebra in the first edition of his work described the peculiarities of a disease which he called "Erythema exsudativum multiforme," and if we pay due regard to these we can easily differentiate between E. multiforme and similar diseases. The author then quotes Hebra's description of E. multiforme, and gives the differential diagnosis between it and E. nodosum, and goes on to say that from the standpoint of the infection theory, E. nodosum is comparable with Herpes zoster, and E. multiforme with a recurring H. labialis. No one will deny the connection between the two processes, but anyone who is a lover of accurate diagnosis will try and distinguish between them.

It is doubtless the superficial similarity in the form of the exanthema which has caused so many observers to include under the name "E. multiforme" or "Erythema" a large group of toxic, reflex, and chronic dermatitides. We are in a position to set up beside Hebra's E. multiforme and nodosum a group of characteristic well-defined types which must be ætiologically, as well as clinically, distinguished from them. Some cases bearing upon this are cited.

Case 1.—Unna was attending a young man in 1877 with pericardial effusion. When the effusion was greatest (no drugs had been used) a peculiar exanthem appeared. A bluish-red papular eruption formed symmetrical semicircles round the angles of the mouth; following this discrete spots

appeared on cheeks, chin, and nose. The spots were symmetrical, and the two corresponding ones always appeared at the same time. The next day the eruption had spread downwards over the neck, and abdomen and arms, and upwards over the forehead. By the third day the disease, always symmetrical, had spread down the legs to the tips of the toes. The individual spots and papules were always separated, arranged in circular incomplete lines, did not enlarge or run together and went through their involution in the same place. Involution began about the fourth day at the angles of the mouth, and spread downwards. By the fourteenth day the exanthem had entirely disappeared. There was no itching. The patient was under observation for a long time afterwards, and there was never a recurrence of the eruption.

This was certainly not a case of E. multiforme. Did the pericardial effusion cause pressure on the sympathetic ganglia of the heart? It was a case of reflex angio-neurosis, but not of the type of Hebra's E. multiforme.

Case 3.—A young healthy man was without any apparent reason attacked by an E. papulatum. The backs of the hands and forearms were affected, but it was remarkable that the trunk was thickly covered with spots and that the eruption was said to have begun here and then to have spread over the whole body. There was no itching; the patient complained only of anorexia.

On the next day some new spots had appeared, and the conjunctivæ were yellow; on the following day icterus was well marked all over, and the urine contained bile, the fæces containing but little. There was no itching at this time. While the icterus increased for some days the exanthem diminished in the same degree, and finally disappeared. Cases of E. multiforme as a complication of jaundice are common enough; but in this case the exanthem appeared as soon as the gall-bladder became distended, and disappeared again as soon as the constituents of the bile entered into the blood.

It was evidently caused, not by the presence of bile in the vessels of the skin, but reflexly by the distension of the gall-bladder; just in the same way as sudden irritation of

the diaphragm (by changes in size of uterus, bladder, bursting of hepatic and diaphragmatic hydatid cysts, &c.) gives rise to erythema and urticaria.

The mode of occurrence of the exanthem, its topography, its sudden disappearance prove sufficiently that this was not a case of Hebra's E. multiforme exudativum but an evanescent reflex angio-neurosis.

Polstebnoff mentions that in his two cases of E. papulatum in jaundice the dorsa of the hands were not affected.

The author gives details of five other somewhat similar cases, and claims to have shown that there are a number of angio-neurotic exanthemata, which are entirely different from, and easily distinguishable from Hebra's E. multiforme.

Following Auspitz, he proposes to call these angio-neurotic exanthemata "Erythanthemata" (ἐρυθρός = red ; ἄνθος = blossom), and defines them as "angio-neuroses of an erythemato-papular type." Urticaria is included in this group, but E. multiforme and nodosum (which Auspitz included in it) do not belong to it ; no more does E. neuriticum, which is a congestive dermatitis, and, as Charcot and Mitchell have shown, somewhat akin to chilblain.

The author in conclusion gives a classification of angio-neuroses :

### Type I. *Anæmia.*

(1) Angio-spasm of the fingers ("dead fingers").
(2) Local asphyxia resulting in necrosis (Raynaud's disease).
(3) Ergotism.

### Type II. *Cyanoses.*

(1) Livedo annularis and frigore.
(2) Perniosis.
(3) Cyanotic form of local asphyxia.

### Type III. *Œdema.*

(1) Acute circumscribed œdema (Quincke's disease).
(2) Urticaria factitia.

## Type IV. *Erythanthema.*

(A) *Symptomatic erythanthema.*
- (*a*) *Reflex*, caused by—
  - (1) Heart disease.
  - (2) Uterine affections.
  - (3) Urethral affections.
  - (4) Peritoneal irritations.
  - (5) Teething (Urticaria infantum).
  - (6) Taste and smell.
- (*b*) *Toxic*, caused by—
  - (1) Bites of insects (Urticaria traumatica).
  - (2) Drugs.
  - (3) Digestive disturbances.
  - (4) Uræmia.
- (*c*) *Infective*—
  - (1) Roseola choleræ.
  - (2) Roseola variolæ et vaccinæ.
  - (3) Roseola infantilis.
  - (4) Prodromal erythemata of variola.
  - (5) Rötheln-like disease of children.
  - (6) (?) Remittent fever with phlyctenous eruption (Wunderlich, Gerhardt, and Heubner).
  - (7) (?) Japanese river-fever (Baelz).
  - (8) (?) Exanthema of meningitis.

(B) *Idiopathic* (*essential*) *erythanthema.* With no known ætiology, therefore clinically divided into—
- (*a*) Erythanthema of maculo-papular form.
- (*b*) Erythanthema of papulo-bullous form.
- (*c*) Erythanthema of urticarial form.
- (1) Urticaria communis chronica.
- (2) Urticaria necrotica.
- (3) Urticaria pigmentosa.
- (4) Urticaria infantum.

## Type V. (?) *Hæmorrhages.*

(A) *Symptomatic*—(*a*) Reflex (in neuralgia, hysterical).
(*b*) Toxic (iodine, salicylic acid).
(*c*) Infective (prodromal hæmorrhages in variola).

(B) (?) *Idiopathic*—Peliosis rheumatica (Auspitz).

ON

# CIRCULAR PATCHES OF EXFOLIATION OF THE PALM AND TONGUE.[1]

*'Exfoliatio Areata Palmæ Manûs et Exfoliatio Areata Linguæ.'*

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The author understands by this a benign disease, limited to the skin of the palms, which has hitherto been, as far as he knows, undescribed.

He saw the first case of this disease in a young girl, on whose palms and digital palmar surfaces circular patches were scattered, as large as sixpenny or shilling-pieces, where the epidermis looked as if it had been punched out.

The bases of these shallow depressions were somewhat smoother than the surrounding skin and somewhat reddened, and the edges were raised. Some were smooth, some jagged, and some undermined. By the coalescence of these circular patches larger areas were formed, especially on the palms. The patient complained of some tenderness over the affected areas, but there was no itching. The usual symptoms of eczema were absent, and treatment directed against that disease failed. A year later he saw a similar case in a man of thirty, who had been ill only a few days—the disease only troubled him through the unsightliness of his hands. There

[1] "Ueber Kreisfleckige Exfoliation der Hohlhand und der Zunge," 'Vierteljahresschrift für Derm. u. Syph.,' 1881.

was no history of syphilis or of any acute illness. A sulphur ointment was ordered, and in two days the man was cured. He saw a third case two years ago, but could form no conclusions as to the ætiology or character of the disease.

He believes that this disease is related to the affection, described by Caspary and others as the "map-tongue," *Lingua geographica*, which occasionally occurs in apparently healthy people. This disease is not of syphilitic origin, and causes the patient no pain or discomfort. Unna describes fourteen cases of the affection which he has had under his care, and distinguishes three degrees of it.

(1) Numerous circular patches, varying in size from a pea to a sixpenny piece, are scattered about upon a healthy-looking tongue. They are mostly discrete, and only occasionally do they touch at their peripheries. They are depressed, and are distinguished from surrounding tissues by their colour. Their usual seat are the margins of the tongue, more rarely the median portions of the upper or under surface.

The edges of the patches are yellowish grey or bluish in colour, the centres slightly depressed and red. The patches tend to disappear suddenly after a few days or hours, while other similar patches may make their appearance. They never creep over the surface of the organ. Their increase in size takes place by the addition of new patches, and not by the enlargement of existing ones.

These patches of exfoliation lie quite superficially in the epidermic layer, and are due to a swelling of the epithelial cells. These cells are more swollen and looser in the centres of the patches, and are therefore more easily removed by the movements of the tongue, &c., the cells at the edges, being less swollen and softened, are less easily removed, and in this way the central depressions are brought about.

(2) The whole tongue, or nearly the whole of it, is affected.

(3) The author has seen two cases of an extreme degree of this affection. The disease extends much deeper, and desquamation is more marked, so that regular ridges and furrows are formed.

He gives details of eleven cases of the affection, and then discusses its ætiology.

He agrees with Caspary that it is not caused by syphilis. Mercurialisation does not give rise to it, he thinks, although one of his patients dated her affection from the beginning of a course of mercurial inunctions; for in six other cases, where the same mercurial treatment was adopted, the existing tongue affection underwent no change, and most certainly got no worse.

Anæmia appeared to be a predisposing cause in one half of his cases. Dyspepsia and bad teeth have no connection with it.

In two of the cases the disease began in early childhood, but it could not be determined whether the children were born with it or not.

The disease may be, he thinks, of neuropathic origin, or a sort of tropho-neurosis. He would define it as follows:—"*Exfoliatio areata linguæ* is a benign disease confined to the tongue, which makes its appearance in circumscribed circular patches which tend to coalesce. It is a painless superficial affection of the epithelium, and the mucous membrane is never affected."

The author then points out the differences between it and

(1) Aphthæ: these cause more loss of tissue, the ulcers are consequently painful; the mucous membrane of the mouth, and gums especially, is affected in this disease.

(2) So-called catarrhal swellings are somewhat like the disease in question, but are more painful, are not so circumscribed, and extend down deeper as far as the prickle-cell area.

(3) Leucoplakia (Schimmer) occurs in streaks and not in rings, is not confined to the tongue, but affects the mucous membrane of the lips and cheeks.

(4) Irregularly occurring exfoliations are usually evanescent, and rarely return; they run a different course, and are due to an irregular desquamation of the whole tongue.

As regards treatment, Dr. Unna recommends sulphur:

℞ Flor. Sulph., 10·0.
Mixt. Gummos., 200·0. M.
Or
℞ Flor. Sulph., 10·0.
Emuls. Amygdal., 200·0. M.

to be used locally. He found the greatest benefit, however, from sulphurous acid, either in the form of a gargle or used undiluted. He recommends the following prescription:

℞ Aq. Sulphurosæ,
Aq. Menthæ, āā 100·0.
Flor. Sulph.,
Syr. Simpl., āā 20·0.
Gumm. Tragacanth., 2·0. M.

The patient, after having cleansed his mouth, takes a mouthful of this mixture, keeps it in his mouth five minutes, during which time he moves it about with his tongue. This may be done several times a day.

# ON A CASE

OF

# CURED LEPRA TUBEROSA.[1]

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GENTLEMEN,—It was my intention to bring before you to-day something unique, viz. a living cured case of tuberous leprosy. The subject is a lady who acquired leprosy two years ago in Brazil, and arrived in Hamburg last December, when she came under my treatment. In this case I have been fortunate enough to cure, according to my view, completely, a disease which until now has generally been considered to be absolutely incurable. She had promised, in an exuberance of gratitude, to accompany me hither to-night, but at the last moment she changed her mind. Fortunately, I had her photographed before and after treatment. In the original picture, front view, you will see that the case is one of leprosy, of rather severe degree. The tuberosities on the side of the face and neck can be seen in the portrait taken in the recumbent position. The photograph taken after the cure will give you an idea what changes one can therapeutically produce in leprosy.

I had last year the pleasure to study, with other German physicians, leprosy in Bergen, under the guidance of Armauer Hansen and of the venerable Danielssen, and it impressed me deeply that with the extraordinarily rich material there at hand, little or nothing could be attempted therapeutically.

[1] "Ueber einen Fall geheilter Lepra tuberosa," 'Separat-Abdruck aus den Verhandlungen des Congresses für innere Medicin in Auftonge der Geschäften-Commission,' Wiesbaden, 1885.

When I inquired into the matter, the general reply was, "We have tried everything that has been proposed, and nothing has been successful; leprosy is incurable!" Danielssen, however, said to me later that if I would come to Norway for a space of time, he would be ready for new experiments. This remark incited me to try everything should I ever obtain a leper to treat, and I had not long to wait for the event. The above-mentioned patient, sent by Herr Schede, entered my consulting-room the middle of last December. The diagnosis was plain, at the first sight, to anyone who had ever been in a Leper House, and there was the characteristic smell, which made a deep impression upon me when I visited the asylums. I have since spoken on this subject with a physician from South America, and he confirms me, and states that it is not difficult to recognise a leper by the smell.

The lady entered my clinique on December 18th, and I have arranged in periods the seventeen weeks during which she was under my care. Before entering upon the treatment, I had designed a plan. It seemed to me probable, from certain histological facts, that the leprous bacilli lived in oxygen, and that without a good supply of this they could not exist. I determined therefore to treat the leprous tubers with the whole series of our modern "reduction remedies," the chief of which are pyrogallic acid, chrysarobin, resorcin, and lastly ichthyol. I mapped out the patient in four skin regions; the right arm I treated with pyrogallic acid, the right leg with chrysarobin, the left arm with resorcin, and the left leg with ichthyol—all in 10 per cent. ointments. I was able to arrive at some conclusions even in eight days. I found that all four preparations had worked favorably, the most satisfactory being chrysarobin and resorcin; the ichthyol had done well but more feebly, and the pyrogallic acid had acted too strongly, it had raised the horny layer into many blisters. For the next experiment I divided the body into two parts, treating the right half with ichthyol, and the left with resorcin—the former drug in a 50 per cent. and the latter in a 20 per cent. ointment. The ichthyol preparation was much pleasanter to the patient, the resorcin causing pain, but otherwise doing well. In a third experi-

ment I tried a purely ichthyol treatment, which lasted for twelve days, and after a few days I began to give the remedy also internally. There was an enormous effect on the skin, and also on those parts which had not been directly treated, especially the eyes. The patient had exhibited that greyish red hyperæmia which is the forerunner of the severe leprous ophthalmia, characterised by photophobia and pain in the eyes upon effort. All these symptoms lessened from the day when the ichthyol treatment was carried out, and the general health ameliorated. The patient arrived in a thin and miserable, and almost helpless condition, caused either by the leprosy itself, or perhaps by an antisyphilitic treatment to which she had been subjected. Although the general health, the appetite, and nutrition improved, it was evident that only a certain point was reached with ichthyol. Many tuberosities had indeed disappeared, but some had left behind them hard remains. I took up the resorcin again; and as the affection was no longer general, but confined to a few places on the skin, I applied the remedy no longer as an ointment, but in the form of "salve- and plaster-mulls." In addition I used a 10 per cent. pyrogallic ointment, but this again proved too strong. As after five days the resorcin had not the desired effect on the hard nodules, a 5 per cent. pyrogallic ointment was used for the whole body.

Now pyrogallic acid is a very dangerous substance. I employ it, indeed, constantly, but I so arrange that only the neck, head, and hands are treated by it, and in consequence of this I have never had a mishap to deplore. The 5 per cent. pyrogallic ointment over the whole body had for some time a good effect, and, becoming bolder, I applied a pyrogallic plaster to the especially obstinate tubers. Unknown to me, the patient covered half of her body with the plaster, with the result of producing alarming symptoms of prostration. In such an event, large doses of hydrochloric acid internally are to be recommended. It is known that the reducing remedies act particularly in alkaline media, and we can weaken their effect on the system by giving at the same time copious doses of hydrochloric acid. In this way I was able to control this severe accident. The invalid was, indeed, feeble for weeks, but on the other hand, the pyrogallic

acid had an excellent effect on the leprous tubers, which almost entirely disappeared. I gave the patient time to recover, only using, meanwhile, milder remedies, so that she gained strength for a final effort, which consisted in a combined treatment with all the four drugs at the same time. Chrysarobin was used from the shoulders downwards, pyrogallic acid on the upper parts, ichthyol internally, and resorcin as a salve-mull to the mucous membrane of the nose. This final treatment carried out for eighteen days gave the result, in my opinion, that the patient was cured. I watched her for three weeks, and during that time only attempted to treat superficial matters—where the skin was somewhat bloated, although not thickened, salicylic plaster was applied, and a mercury plaster to remove pigmented spots.

You perceive, gentlemen, that with care and energetic treatment much can be attained in this disease. The case was a somewhat severe universal one of *lepra tuberosa*, the arms and legs were, indeed, extensively attacked, and the eyes and nose were affected. I cannot say whether any affection of the internal organs was present. The treatment was not only external; moreover the application of the above remedies to the skin is constitutional, for all these drugs become absorbed. The disease having so obviously disappeared from the skin, we may well imagine that the visceral leprosy is also cured. We cannot even declare to a syphilitic patient that he is absolutely cured of his disease, although we may promise that every subsequent attack can be similarly cured. If we can attain to so much in leprosy, I think that we have accomplished what we may provisionally quote as a cure.

# SYPHILIS AND ECZEMA SEBORRHOICUM.

As this important paper has already appeared in English in the 'British Journal of Dermatology,'[1] an abstract only will here be given. The author in the first place alludes to the careful work of Fournier and others, who have shown that the polymorphism of the syphilides may be resolved into a series of clinically recognisable fixed types which are influenced by various conditions.

The well-known though infrequent form of acneiform syphilide, hitherto looked upon as a simple type, may really be regarded as a mixed infection—a papular, follicular, or lichenoid syphilide which has become simultaneously infected by a pus-forming coccus; for suppuration is not a character of syphilis. We must, moreover, regard a number of other well-known syphilides as mixed infections of syphilis and *eczema seborrhoicum*.

The author's attention was first directed to the co-existence of these two exanthems in attempting to diagnose certain doubtful cases of so-called "corona veneris;" and a like symbiosis was recognised in many other cases of papular or crusted-papular, and especially of serpiginous syphilides of the late secondary stage. Whenever secondary syphilis presented itself, it corresponded in its distribution and inflammatory intensity with the seborrhœic process.

Three grades of the latter may be distinguished; one slight, the others more severe. It almost always commences

[1] 'British Journal of Dermatology,' vol. i, Nos. 1 and 2, 1888. "Syphilis und Eczema Seborrhoicum, 61 Naturforscherversammlung in Köln," 'Monatsh. f. prakt. Derm.,' Bd. vii, 1888, No. 217.

as a squamous eruption, with but slight inflammatory character, and easily escaping notice. There may be defined, circular, pale or reddish, scaly spots (pityriasis capitis, barbæ, faciei, corporis) ; slightly raised, irregularly bordered or coalescing, yellowish-red, scaly papules (eczema seborrhoicum, papulosum corporis, rosacea seb. faciei), or regularly formed, serpiginous, yellowish-red, papular plaques or rings, with eroded edge and yellow depressed centre (ecz. seb. annulatum, sterni, dorsi, and flexuosum, and certain ecz. marginata nuchæ).

From these squamous forms the others may develop by intensification of the inflammation ; and thus we may get, on the one hand, the scabbed or crusted varieties (many cases of so-called psoriasis gyrata and annulata, and many dry eczemas), or, on the other hand, the weeping varieties (ecz. seb. madidans capitis, aurium, genitalium, flexuosum). The crusted forms are particularly associated with the ringed squamous variety, and the weeping forms with the papular.

In whatever way seborrhœic eczema manifests itself, it is able to prepare the ground for the papular syphilide, and to bring on that eruption.

The papulo-crusted syphilide (s. papulo-crouteuse of Fournier), which always occupies the favourite sites of seborrhœic eczema, viz. the scalp and face, is a striking example of mixed syphilis and eczema seborrhoicum. The yellow seborrhœic edge spreads chiefly on the temples and brow, extending beyond the papules, which under the syphilitic influence become larger, more raised, flesh to copper coloured, and pigmented. The crusts are dry and fatty. In the hairy scalp, beard, and mons Veneris, the crusted papules here and there coalesce, and form raised masses, depressed in the centre and with sharp serpiginous borders. The mingling of the two affections is particularly well marked in the naso-labial furrows—the area of hyperhydrosis oleosa —where large sweat-glands exist which may become affected with seborrhœa and inflammation.

On other parts of the body, particularly on the legs, serpiginous papulo-crusted syphilides chiefly occur. The secondary papular syphilide has in itself no tendency to spread in a circinate manner, although the papules may

become confluent, and portions of skin may become invaded by a continuous growth of young papules between the older ones. An uninterrupted uniform advance indicates an affection of the epidermis or of the papillary layer of the corium, for these are the only layers of the skin which have a uniform structure in all regions; and unless there be necrosis, lesions of the cutis do not proceed in a uniform serpiginous manner. Hence it is not extraordinary that seborrhœic eczema, creeping on in the superficial layer, assumes a serpiginous character, which the papular syphilide by itself does not.

A hyperæmic condition of the cutis, no doubt, influences the development of a syphilide, which will always appear in those parts of the skin which have been irritated. Thus a miliaria rubra can determine the onset of a small papular syphilitic rash, and an attack of scabies may promote an eruption in the interdigital folds and gluteal regions.

The author lays down the proposition that "a serpiginous parasitic eruption of the upper skin is able to impress the eruption of a syphilitic exanthem with the stamp of a truly serpiginous lesion, in that it, by its continual progression, keeps rendering new and hitherto healthy ring-shaped tracts of skin fit for the development of syphilides." He gives a case in illustration, in which the patient had been the subject of seborrhœic eczema, and had subsequently acquired syphilis with the development of a typical serpiginous, papulo-crusted eruption on the neck.

That form of syphilitic so-called "psoriasis palmaris" which gradually appears late in the secondary period, spreads in a serpiginous manner, and is so resistent to constitutional treatment, is an example of the mixture of an obstinate seborrhœic eczema of the palm with a papular syphilide.

Another mixed form is observed in the scalp, where an ordinary syphilitic alopecia may be accompanied by scurfiness and small itching papules. A nummular syphilide on the forehead, nose, or cheeks may also unite with slight seborrhœic rosacea to form large dark red papules or patches, which must be locally treated in order to ensure rapid disappearance.

Weeping seborrhœic eczema, combined with syphilis, explains the so-called "syphilis vegetans." The moisture of

these condylomatous outgrowths has usually been ascribed to uncleanliness, and to secretions from adjoining parts. But the growths also occur in the anal region, the axillæ, and even on the hairy scalp; and whatever effect the above conditions may have, these positions are certainly sometimes the seat of seborrhœic eczemas. The presence, indeed, of oozing, exuberant papular syphilides on the scalp is a sure sign of the mixed infection.

Certain cases make it probable that some tertiary tubercular syphilides are likewise developed upon a seborrhœic basis; such, *e. g.*, as the serpiginous ulcerating or non-ulcerating forms on the face, scalp, neck, breast, and axillæ. The author believes that here, too, the serpiginous character is determined by the seborrhœic eczema.

Secondary syphilides resemble seborrhœic eczema in showing a preference for the flexor surfaces of the extremities, as well as the head and genitals. The eczema keeps up in these situations a slight but continuous irritation, and a hyperæmia which can be at any time intensified. When a patient so affected becomes syphilised a "facies seborrhoica" is impressed upon the syphilide.

There are, however, many morphological, subjective, and therapeutic differences between the two pure diseases.

The syphilitic papule tends to be sharply circumscribed, remains not bigger than a pea or lentil, is never very scaly, but frequently quite smooth and merely surrounded by a fringe of scaly epithelium, and it is stiff and elastic to the touch. It is generally of a dull brownish-red tint, and pigment is often deposited in its site and in its neighbourhood. Although, when numerous, there may be some confluence, there is no regular continuous serpiginous character. It never itches or smarts; and, apart from the head and genitals and flexor surfaces of the limbs, it is mostly seen on the front and sides of the lower parts of the trunk. Syphilides come out approximately at the same time over all parts of the surface attacked; and they yield promptly to mercurial treatment, but not to such applications as sulphur, resorcin, or zinc oxide.

The seborrhœic papule, on the other hand, is only circumscribed in special localities (sternum, axillæ, forehead),

generally has irregular outrunners, is variable and more polymorphic in character and extent, and is always more or less scaly or even crusted. It is not dense and elastic; in colour it is yellowish red, with a characteristic yellow tone around, and without pigmentation. In addition to the regions common to both affections, it prefers the sternum, the interscapular space, and the sacral region. The course of the eruption is slow, from above downwards, and it is frequently limited to the upper parts. It readily yields to sulphur, resorcin, and zinc oxide.

An interlocking of the seborrhœic and syphilitic processes may therefore be assumed when (1) the separate spots are very various in size, confluent, and not sharply defined; (2) the specific syphilitic colour is replaced by a fresh yellowish red; (3) the greater part of the papules are covered with scales and fatty scabs; (4) the arrangement is serpiginous; (5) a yellow colour is present around and in the centre of the serpiginous circles; (6) there are eczematous characters, oozing, heat, and tension; (7) there is itching of greater or less intensity; (8) the eruption occurs on the scalp margin of the forehead, in the naso-labial furrows, on the sternum, between the shoulder-blades, and over the sacrum; (9) it is concentrated on the hairy regions, or on places of contact; (10) the eruption is unusually obstinate to constitutional treatment, but improves under local antiseborrhœic applications.

The practical deduction is that "whenever we recognise, in accordance with the above-mentioned signs, the co-existence of a syphilide with the seborrhœic process, or wherever we find a purely seborrhœic eruption side by side with a syphilide, the treatment must consist from the very first in the application of an antiseborrhoicum locally, in conjunction with the general internal administration of mercury or iodine."

# LICHEN RUBER AND ITS TREATMENT.[1]

From an experience of thirty cases met with in four years, the author is enabled to compare the various forms of "Lichen" with the descriptions of German, French, English, and American authors. He gives notes of fourteen cases and the treatment adopted, and discusses at considerable length the views of Wilson, Hebra, and many others.

He divides "Lichen ruber" into *L. acuminatus*, *L. obtusus*, and *L. planus*, the papule in the first being acute and pointed, in the second obtuse, and flat in the third. The papules in all varieties have the common characters; they have a livid, bluish or yellowish-red tint, a hard consistence, a peculiar dryness, they are more or less itchy, and more or less persistent. They never become vesicular or pustular. At times, when the disease is universal, the different forms may be combined.

*L. acuminatus* consists of small papules 1 to 1·5 mm. in diameter, the size of a millet or mustard seed, conical, and covered at the point with a small, scaly, intensely itchy elevation, which corresponds to the orifice of a hair follicle. When the skin between them reddens, swells, and becomes thickened, they may appear confluent, forming large plaques. The itching is more severe than in the other varieties. The affection generally sets in acutely, after profuse perspiration, chill, or rigors. Properly treated, it may be localised and cut short; otherwise it may extend all over, and become chronic, and lead to death from marasmus, &c. Hebra's

[1] "Zur Klinik und Therapie des Lichen Ruber," 'St. Petersburger medicin. Wochenschrift,' No. 45, ff, 1884; and "Clinical History and Treatment of Lichen Ruber," 'Med. Bulletin,' Philadelphia, 1885.

treatment by large doses of arsenic takes long to act; Köbner's arsenic injections have a somewhat quicker effect, but the most rapid and agreeable method is by carbol-sublimate inunctions, which may cure recent cases in a week, and older ones in two to four weeks; the itching diminishes almost from the first day.

*L. obtusus* consists of papules 3 to 5 mm. in diameter, raised but flattened on the top, with a small indentation in the centre, hard, dry, waxy, and translucent, bluish- or brownish-red and without scales. It is less acute, less itchy, and more circumscribed than *L. acuminatus*. Left to itself it may spread, but then leaving large intermediate areas of healthy skin. The neighbouring papules may form together large plaques; and, when cured, brownish pigmented, thin, scar-like spots remain. Hair and nails never suffer, nor does it end in marasmus. Arsenic has less effect, but it may be quickly cured by the carbol-sublimate inunction, or single papules may be removed by strong paints or plasters of chrysarobin, sublimate, or salicylic acid.

*L. planus* shows perfectly flat red spots, but slightly elevated, depressed in the centre, and 6 mm. to 4 cm. in diameter; the surface is smooth, or often with a thin scale. They may develop either by a coalescence of very small, flat papules, or by a gradual increase in size of a single spot; they may also be formed from "obtusus" papules which are commencing to heal, and even from a group of "acuminatus" papules. Thus there may be primary and secondary "planus" papules. Their character is due to the fact that the papillary area is evenly affected, while in acuminatus and in obtusus the parakeratosis is more apparent in the former in the hair follicle, in the latter in the sweat-pore. The planus papules are more prone to remain isolated, and they increase more slowly and do not influence the general health. Arsenic has less effect, but the isolated spots have been cured by mercury and arsenic plaster-mulls, sublimate and salicylic collodions. In this form, superficial bullæ may at a late period appear. Much that has been described in England and America as "Lichen planus" is *L. obtusus*.

The author gives an historical and critical review of the whole subject; comparing the original descriptions of F.

Hebra's "Lichen ruber" (1860) and Erasmus Wilson's "L. planus" (1869), and maintaining that the former observer was acquainted only with the "acuminatus" variety, while the latter only knew the "obtusus" and "planus" forms—especially the first. He refers to the remarks of Tilbury Fox, Piffard, Robinson, &c., in England and America, and of others in Germany and France. He has had no personal experience of Weyl's "L. acnéïque or L. circinatus" nor of Vidal's "L. corné" and Chambard's "L. hypertrophique;" and he admits that we are yet far from a complete knowledge of the lichen group.

The author's original carbol-sublimate ointment consisted of—

Ung. Zinci Benz., 500.
Acid. Carbol., 10—20.
Sublimate, ·5—1.
With or without Ol. Olivæ, 20.

# HYPHOGENIC, COCCOGENIC, AND BACILLOGENIC SYCOSIS.[1]

THE author refers to the progress made in dermatology through the principle of parasitism, even in connection with those diseases which have been long ascribed to micro-organisms. We cannot now say that a particular fungus, like Trichophyton, is the cause of a trichophytosis without absolute demonstration, viz. isolation, inoculation, and cultivation.

Sycosis furnishes a striking example. The idea of a differentiation of sycosis into a parasitic and non-parasitic form is now obsolete. Since, indeed, Bockhart in 1887 showed that pus cocci could produce the typical phenomena of the disease we know that all sycoses are parasitic. The two forms hitherto described are the hyphogenic and coccogenic; but a third form has lately been demonstrated by Tommasoli, in the author's laboratory, to be bacillogenic.

Hyphogenic sycosis (*herpes tonsurans barbæ*) starts in the hair itself, the fungus—not developing in liquids—being in the narrow clefts between the horny cells, beyond the region where the lymph circulates. Staphylococci, on the other hand, attack the hair-bulbs in a very different manner; they thrive in the lymph-spaces, and afterwards invade the fibrous and epidermic structures of the follicle. This is rendered possible when they get into the space between the hair and the root-sheath, when the cleft which is normally closed above (Pinkus) is mechanically opened. The hair never becomes brittle, as in the hyphogenic form, but kinks up, and epilation is painful. The tubercles which result are

[1] 'St. Louis Medical and Surgical Journal,' August, 1889.

smaller, harder, more hot and painful, and lie entirely in the cutis; and inflammation of the entire cutis may ultimately ensue. The hyphogenic folliculitis is more acute, and spreads from hair to hair, only stopping at the scalp; and for this reason, while the fungus may be closely allied to *T. tonsurans*, it may not be identical. Coccogenic sycosis is everywhere endemic, hyphogenic epidemic; any suppuration may give rise to the former, but only specific inoculation to the latter. The hyphogenic form is easily cured, even by weak parasiticides; the coccogenic most difficult to treat—the best results being by a therapeusis of exclusion. If left to itself, the latter may lead to the total suppuration of the follicles with the formation of scars, *i. e.* if the prickle-layer of the lower part of the hair-bulb be attacked.

In old cases a coccogenic sycosis may be superadded to a hyphogenic; and it is questionable whether the large tubercles of the latter be not due to an infiltration of cocci.

From an apparently mild case of sycosis in the author's clinic, Tommasoli obtained a pure culture of bacilli with no admixture of pus cocci. The rods were short, rather thick, elliptical, and with rounded ends. They did not liquefy gelatine; and by inoculating with a needle, yellowish-white "nail"-cultures with smooth heads were developed. They grow best on potatoes as a thick mucoid growth and with a green discoloration around, and with unpleasant odour. It is distinguished from *B. parvus-ovatus* (Höffler) by being innocuous to rabbits, and from *B. pyogenes-fœtidus* (Passet) by its whitish-yellow colour on potatoes. The author and Tommasoli name it *Bacillus sycosiferus-fœtidus*. On inoculating skin, typical sycosis appeared, with red indurated papules at the sites of the hair-bulbs, with small apical pustules, painful to the touch and on epilation. Pus cocci as well as the bacilli were found in plate-cultures from the pus.

It is probable that some of the mild cases of supposed coccogenic sycosis are really bacillogenic, especially where there is mild interfollicular disease with scanty suppuration.

The rapid development or revolution in the study of sycosis during the last few years illustrates the value of systematic experiment.

# THREE VARIETIES OF FAVUS.[1]

THE original paper on this subject was read at Halle in September, 1891, before the dermatological section of the sixty-fourth meeting of German scientists and physicians.

The following is a short abstract. Through the work of Quincke the study of favus has received a great impulse, and the facts which have now come to light show how very short-sighted we have been in the past with regard to our clinical observations of this disease.

Dr. Frank recognised that among the collection of favus in the author's laboratory there were three different varieties. Experiments, numerous and varied, were then undertaken to determine the exact differences which the diseases produced by the various fungi presented clinically. The fungi were numbered I, II, III. Dr. Frank inoculated himself with a pure culture of No. I, obtained from mice. In three weeks the disease was clearly established. At the author's request Dr. Williams inoculated himself on the leg with fungi I and III, at a little distance apart. The skin of the leg was chosen because the author had observed how firmly favus adheres to the skin in this region. On the third day following inoculation from No. I the part was inflamed; on the fourth day some minute vesicles had formed; on the fifth the whole surface of the inoculated patch was swollen and painful on movement; on the sixth day crusts began to form, and great pain was experienced; so great was the discomfort that the horizontal position had to be maintained. The site of inoculation with No. III caused by far less serious symptoms, and developed more slowly. Throughout their whole course the two inoculated

[1] "Drei Favusarten," 'Monatsh. f. prakt. Derm.,' Bd. 1892, No. 1.

patches exhibited distinct differences. 1. The scutula of Favus I were less numerous, and not so concentrated as those of Favus III. Some of the scutula of Favus I formed only half-rings, whereas Favus III was specially disposed to build up typical cupped crusts.

2. Scutula of Favus I were greyish yellow, while those of No. III were dark sulphur-coloured. The former presented much the appearance which we find in the ordinary favus of mice.

3. Scutula of No. I were much softer and more brittle than those of No. III.

4. Scutula of No. I adhered more firmly than those of No. III to the horny epithelial substratum. The above characteristics were sufficiently well marked to enable us to differentiate the two affections with ease.

The author was the sixth of those who inoculated themselves with fungus No. II, the result being negative in each instance. White and black mice, white and black rats, guinea-pigs, rabbits, cats, and chickens were inoculated with the three varieties of favus. On white mice and rats, black rats and chickens, the fungus did not take effect well, at least no typical scutula were developed. Throughout the numerous inoculation experiments, however, the differences between the scutula formed by each variety were maintained.

Microscopic examination also showed individual peculiarities of growth upon the skin, as well as differences in the filaments of the fungi themselves and their mode of sporing.

For the fungus of No. I the name proposed is "Achorion enthythrix" (*i. e.* possessing straight running hairs). For the disease produced by it the term "Favus griseus" is suggested, on account of the greyish-yellow colour of the scutula. The term "griseus" is apothecary's Latin, but has the advantage of being more easily understood than *ravus*, which would be more classical. No. II the author calls "Achorion dikroön" (not to be confounded with dichroön), on account of the forked ends of the hyphæ. The disease will be termed in future "Favus sulphureus tardus," owing to its sulphur colour and slow growth.

For variety No. III the term "Achorion atakton" appears suitable, in consequence of the irregular course of

the hyphæ; and the disease which it produces receives the name "Favus sulphureus celerior," because the crusts are of a sulphur-yellow colour, and the growth of the disease is relatively quicker than that of No. II.

Three practical points are specially referred to with respect to the study of the fungi cultivated on artificial media.

1. In order to remove any doubt as to the real difference between the various fungi, they should be grown upon the same plate. If cultivated closely alongside each other, they can be stained, cut, and examined microscopically upon the same slide and in one section.

2. The best cultivating material so far has had the following composition:—Agar, 4 per cent.; peptone, 1 per cent.; levulose, 5 per cent.; common salt, ½ per cent.

It requires a steam filter for its satisfactory preparation, and should be put through it twice.

3. For obtaining pure cultivations, the employment of a rather dry nutrient material is recommended. It is also advisable not to neutralise the agar, but allow it to remain slightly acid. In this way the favus can more easily outgrow the development of any micrococci present. Cultivations from the crusts are obtained by taking a small portion from the middle of the latter and smearing it upon the drier upper end of the agar in a sloping tube.

To obtain cultivation from hairs, their free ends should be singed off up to near the roots, and the latter then transferred to the agar, being placed upon the dry upper end of the tube.

According to the author's experience, the following is the best method for protecting and transporting favus material intended for cultivations. A piece of good sticking plaster is pressed upon the closely clipped favus patch, which should first have been well washed with soft soap or otherwise disinfected. After a time the plaster should be plucked off, when it will be found to have extracted numerous hairs, many of which carry the fungus. The plaster should now be attached to the lid of a sterilised tin box, and the box closed so that the hairs hang free. Preserved in this dry condition, cultivations can be obtained satisfactorily after the lapse of some weeks.

From the results of eight attempts to produce favus on the non-hairy parts of adults with fungus of *F. sulphureus-tardus* the author concludes that this variety probably only excites on man a short-lived superficial disease, known as "Favus herpeticus."

The cheeks of the common house-mouse were inoculated with the three forms of fungus, and exhibited well the points of difference between the scutula which form in each case. Some of these distinguishing characteristics are as follows:

*Favus griseus.*—Scutulum of moderate size, about that of a lentil, and as thick. On the upper surface flat or raised, not cup-shaped. Grey-yellow, like old wash-leather, neither shining nor smooth. Penetrated at all points by the fine and tactile hairs.

*Favus sulphureus-tardus.*—Scutulum very large, covering the whole cheek, and thick. Cup-shaped on the surface, and covered by small humps, gathered into folds, yellowish white, cream-coloured, smooth as leather, shining in some parts, and pressing back the hairs, which do not penetrate it.

*Favus sulphureus-celerior.*—Scutulum remains small, about the size of a peppercorn, cup-shaped on its surface, smooth but not shining; of a light ochre-colour towards its periphery, in the centre whiter, and on the folded margin of a horn-like brown. It presses back the finer hairs, but is penetrated by the larger. [A. E.]

# RECENT ADVANCES IN THE THERAPEUTICS OF THE SKIN.[1]

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At the request of the publisher of the journal,[1] Dr. Unna sketches the present position of Dermato-therapeutics, limiting himself to the most important skin diseases, but going with exactness into those details interesting to the general practitioner.

Since 1881, when the late Oscar Simon wrote on this subject in the same journal, the principal matters to note are improvements in the technical methods of therapeutics; and these may be illustrated by a few typical examples. They belong more to general therapeutics, and are of importance to every practitioner. Indeed, the treatment of slight but troublesome skin ailments has gained more by these technical methods, than that of the severe dermatoses which come before the clinics and specialists. Before entering into these new therapeutic measures, we may consider the new medicines which have been able in the last few years to gain a certain position. They are salicylic acid, the ichthyol preparations, calcium sulphide, resorcin, and cocain.

Until its invaluable keratolytic property was discovered, salicylic acid was only used by dermatologists, in weak doses, as a means of killing fungi. We have hitherto possessed no drug which will remove so well and quickly the normal, or pathologically thickened, horny layer. The dose, indeed, for this purpose must be particularly strong, and moisture must be excluded. These conditions are only properly combined in the salicylic plaster-mull (5, 10, 20, to 50 grammes per

[1] 'Aerzlichen Vereinsblatt für Deutschland,' 1885, No. 158.

roll); hence, a constantly increasing interest in this preparation has lately arisen in all countries. The most obstinate circumscribed dermatoses, strongly infiltrated patches of eczema, psoriasis and lupus, can clearly be treated locally, with much greater prospect of result, after the epidermis has been thinned by means of salicylic plaster-mulls. It differs from all other hitherto known substances of the kind, in its action, however intense, being limited to the horny layer alone. The prickle-cell layer of the epidermis is never affected; and, therefore, so long as it is used alone, vesicles and blisters never form, as *e. g.* with sublimate. Its keratolytic action is in no way an ordinary corroding one; the salicylicated horny layer can be scraped off as a soft, whitish, compact membrane.

This point is mentioned at length, because it will doubtless be of great importance in the dermato-therapeutics of the future; there is enormous advantage in thus being able to commence the treatment of obstinate circumscribed skin diseases. At the same time it is possible that we may discover other potent drugs for the same purpose, by studying the peculiar chemical action of the salicylic acid.

But salicylic acid does more than this. Under its action infiltrations and granulations disappear, just as well as with caustics and alkali soap, which until now were our chief means of obtaining these results. Naturally in a concentrated form it affects deleteriously many skin parasites; and hence mycotic eczema of long standing can be attacked by nothing more quickly and surely than by strong applications of salicylic acid. Lupus infiltrations are affected by it in the same way as by arsenic and mercury: while psoriasis patches are certainly thinned, although not cured, as with chrysarobin. As a rule, when a universal dermatosis shows especial obstruction to treatment on account of the firmness of the epidermis, 2 per cent. to 5 per cent. of salicylic acid may be added to the remedies otherwise indicated, in order to obtain a quicker action. The salicylic acid can be combined unlimitedly with almost all our drugs, with the exception of alkalies and soaps.

The value of sulpho-ichthyolate of ammonia (soda, &c.) lies in its large percentage of sulphur, its solubility, and its

absolute indestructibility. As it easily blends with the tissue juice, and can be continuously taken internally without danger, very considerable and unusual effects of sulphur can be attained by its means. Like the usual sulphur remedies it has a favorable local action on horny anomalies (Parakeratoses), and so especially on pityriasis simplex (Alopecia pityrodes), Seborrhœa sicca, ichthyosis, and desquamation after acute exanthemata. In slighter cases of psoriasis, a favorable effect is also unmistakable. While the usual sulphur preparations can only be used with care in eczema and by constantly watching their action, a weak addition (2 per cent.) of ichthyol salt to the most useful anti-eczematous remedies, acts well under all circumstances, and quickens the drying up, particularly in the much crusted eczema of children. The internal administration of ichthyol (grm. 1·0 per diem, 0·2 to 0·5 for children) is of still more importance, particularly in all those eczemas which we must ascribe to nervous origin. To this class belong the dentition eczemas of children, *Lichen urticatus*, leading to pruriginous eczema, the commencement of true prurigo, and those eczemas of adults with circumscribed herpetic characters, by choice localised in the region of the radials and remarkable for their symmetry and pre-eminent tendency to relapse. In these cases, ichthyol deserves to replace the commonly used arsenic —which it will probably supplant. It is also of great use as an anticatarrhal just after leaving off arsenic, when the latter cannot be borne.

The principal rôle, however, of ichthyol salts is played in acne, which is also to be classed among the corneous anomalies, and in rosacea. The firm horny layer and the obstructions of the follicular mouths disappear under its influence just as quickly as the enlarged vessels and the thickenings of the cutis. It is a special advantage that we can here use sublimate at the same time, as it is not contra-indicated with this sulphur remedy.

Finally, the ichthyol preparations have proved themselves useful as external applications in certain infectious skin inflammations, particularly in *furunculi*, erysipelas, lymphangitis, and panarites, also in acute exanthemata, and lately, moreover, in leprosy.

Calcium sulphide, a very old remedy, which on account of the uncertainty of its preparation, and from the results of decades, was long left in oblivion, has been again lately recommended by English authors. It is a reducing remedy of great effect in interstitial suppurations, especially at their beginning, and should be given internally only in small doses (grm. 0·005—0·01, three to four times a day). It should, of course, be as pure as possible, carefully prepared, and subsequently preserved in charcoal. Pleasantness and certainty of action, however, are only guaranteed when the remedy is given in the form of "small-intestine pills"; and from its uncommonly easy decomposition by acids it forms a sure means of testing the insolubility of such a pill in the stomach. After its administration there should be absolutely no eructation of $H_2S$—such as occurs when given in other ways.

Resorcin, as an acknowledged anti-putrefactive remedy, was first tried in infective skin diseases; and indeed it has well justified our expectations. From its freedom from smell, it is preferable to the ichthyol preparations in acute processes, like common erysipelas (in 10 to 20 per cent. ointment), lymphangitis, &c.; but as it is not quite so harmless, we can only apply it with care in universal and chronic skin affections. A favorable result has been obtained with it in all the parakeratoses, including psoriasis and pityriasis rubra. Among eczemas, also, there are some which clinically present a parasitic character, and for these, resorcin is the best remedy. To this class belongs that dry very itchy eczema of the eyelids, which easily passes on to fissures, and is typically accompanied by a similar form around the mouth, anterior nares, and sometimes the scrotum—a rare but serious kind of multiform eczema. Resorcin, as an ointment, of 10 to 30 per cent., here rapidly leads to a cure. The rôle of this drug will probably soon be enlarged, for it has only been recently introduced in the therapeutics of skin diseases.

Cocain here deserves mention, although it is only a quite recent acquisition. There are two troublesome affections in particular for which it is already used, and with great success, in a 1 per cent. solution or 1 per cent. ointment. These are the painful fissures of the anus and nipple.

Cocain is at present the only remedy on which we can confidently recommend mothers and wet-nurses to continue suckling, even when there is soreness and fissure of the nipple.

To these chemical remedies, which are selected as by far the most important of those most newly introduced, we may add two physical house remedies which are always at hand; viz. hot water and the powder bag.

The uses of hot water, and its comfort to the patient if properly applied, are so considerable, that it is surprising that dermatologists have not hitherto adopted it to the same extent as the gynæcologists. Thanks to the example of the latter, it has now, however, been lately adopted by us. A sponge is dipped into water just hot enough to be borne by the patient's hand. The sponge, partially squeezed, is then firmly applied to those parts of the skin which are hyperæmic, weeping, irritating, or bleeding, and, in spite of the smarting from the heat, kept on for about half a minute. This proceeding may be repeated several times at short intervals. The damp skin is then exposed to the air, or powdered, if it be desired to increased the cooling effect; and in either case, when dry, all rubbing must be avoided.

Patients with rosacea, who frequently suffer from flushes of blood to the head, are most thankful for the recommendation of these deterent hot applications. Their instinct has rarely led them to combat their symptoms with hot water; for they usually indeed wash as often as possible in cold water, which although of momentary comfort always makes the evil greater —the primary contraction of the vessels producing, as a reaction, a lasting paralysis. After every meal, excitement, or exertion a short hot bathing is especially advisable. If the hot sponging be continued too long, the effect is not so considerable—the subsequent contraction of the vessels being lessened.

We proceed in a like manner if we wish to stop the bleeding quickly after scarification for lupus, rosacea, &c.; if, however, the bleeding is to be promoted, the water should be of a temperature of 20° to 25° C.

The hot sponge acts particularly well in all itching affections, without exception. In Pruritus ani and scroti an immediate result follows; and as in these cases the itching

is just most acute when dressings have been on for some time and must be changed, it is well to rapidly bathe the parts with hot water immediately before applying the fresh dressing (salve, plaster-mull, or jelly). In all affections also, accompanied by a thickened horny layer (acne, psoriasis, &c.), hot bathings are the best; we may indeed lay down the rule that they are preferable to cold in most diseases of the skin.

A remedy, also of simplicity, which only recently has begun to be valued, is the powder-bag. Every physician in his daily practice, meets with a number of circumscribed obstinate skin affections, particularly of eczematous type, in which, from maltreatment on the part of the laity, it is often difficult to determine what is the true affection and what is superimposed irritation. Moments, moreover, come to the physician in the treatment of such diseases, when it is hard for him to decide whether a sudden turn for the worse, or a cessation of improvement, is to be attributed to a remedy or to the disease itself. In such cases, the application of the powder-bag soon brings back the affection to its natural condition, and then it may be more clearly known what had best be done.

Many eczemas are quite cured by this treatment, after they have previously defied the ordinary measures. The powder-bag is as useful for simple powdering as the salve-mull dressing is for simple inunction. It represents the most concentrated action of a simple powder, all the more because any sort of meal filtered through the bag deposits a dust-like powder of greater fineness than that of even the very best powder which can be bought.

The bags should be made of old used linen, or other material not too dense, the pieces being evenly cut and sewn together in the form of a bag, except at one border—which remains open for filling with a moderate amount of simple rice or potato meal. After closing, the bag is sewn with quilt stitches through and through, in order to keep the meal evenly distributed; and it is then tied directly on to the skin. Fats must not be applied to the skin at the same time, as they stop up the pores of the powder-bag. For arms and legs, we take two pieces of sleeves, thin stockings, drawers, &c., one placed inside the other, with the space

between filled with powder; for the genitals the bag is fastened on with a suspensory bandage; a trunk bandage is used for the body, and whole masks, in the form of a bag, can be constructed for the face.

Turning now from the simple remedies to the few dermatoses in which improvement can be shown under the new methods of treatment, we may commence with eczema—to which, as the chief representative of these skin affections in which the barrier between the tissue juice and the outer world is broken down as in surgical wounds, the first real attempts were naturally directed after the perfection of surgical technique gave the first impulse to these advances. As these attempts were quickly crowned with success, a rapidly developing reform ensued of our whole healing apparatus.

The first step took the form of salve-mulls, which continued the old principle of fatty applications. Instead of lappets of cloth covered with ointment, as recommended by the elder Hebra, we have ready at hand for the patient a plastic plaster, which can be cut and folded according to will, consisting of the lightest bandage-mull impregnated with ointment. After a mass of rich experience, we may regard the use of salve-mulls for all circumscribed eczemas of the face, ears, nostrils, arms, hands, feet, and legs, as well as the genital organs, as one of the best and most effective methods of treatment. The more complicated the surface, the more apparent are the advantages; and for this reason they are especially useful for the conchæ and nostrils—eczema of these parts now taking by their means half the length of time for cure. The extremities and neck can also be advantageously treated with them; but not the trunk, and universal eczema, on account of the cost. Binding-mull of different widths may usually be used for keeping on the salve-mull, and, if softening of the skin is to be promoted, a piece of gutta-percha tissue may be inserted between the salve-mull and the mull binder. The most useful forms for these eczemas are the "zinc-ichthyol," the "zinc-salicylic," the "zinc-thymol," the "zinc-sublimate," the "zinc-red precipitate," the "white precipitate," the "lead-carbolic," and the simple "boric," "lead," and "zinc" salve-mulls.

For circumscribed patches on the face and back of the hand, the salve-mull can be prepared only on one side, so that it can be pressed on, outwardly presenting a dry surface, and retained without bandaging.

If the salve-mulls leave anything to be desired it is that (1) they do not alone possess sufficient adhesive power to hold on, and (2) that they do not absolutely dry outside. A considerable technical advance was made by using in their manufacture two materials of conspicuous adhesive power, india-rubber and oleate of clay, the former being inert with regard to the disease, and the latter showing anti-eczematous properties. The "plaster-mulls" thus made stick admirably, and are perfectly dry on the surface—characters which have made them much liked.

Two plaster-mulls have shown themselves especially suitable for eczema, the "zinc" and the "salicylic" (5, 10, 20 grms. per roll). If the salve-mulls, through their fatty constituents, keep back the watery exudation of the skin, this effect is still greater when plaster-mulls are used—and herein lies their strong, as well as their weak side. It is difficult to imagine an application which guarantees a deeper action of the medicaments. The remedy is enclosed in these plaster-mulls, in a pure, almost undiluted condition, between the epidermis and an absolutely water-tight, firmly-adherent membrane. The diffusive conditions of the horny layer are in consequence quite novel, and by far more favorable. Swelling as it does from the excess of the warm skin vapour, and becoming almost like a mucous layer, the soluble and volatile ingredients of the plaster pass in a weak but uninterrupted stream from the lower surface of the mull into the skin. Hence these plaster-mulls are indicated in obstinate circumscribed skin diseases, in diseases of deep-lying organs (muscles, tendons, joints, bones, serous cavities, testicles, larynx, &c.), and as agents for the treatment of chronic constitutional diseases (syphilis).

On the other hand, in consequence of being waterproof and soddening the skin, they could scarcely be expected *à priori* to be of much use in eczema. As a matter of fact, however, the zinc and salicylic plaster-mulls are of especial value in eczema, and this shows that their energetic deep action quite

compensates these collateral effects. Whilst the zinc plaster-mulls suffice for the superficial slight eczemas (*e. g.* of the fingers, hands, and face), the salicylic mull should be used for all severe cases, in a strong form at first, and in a weaker form at a later period.

The concentration of fatty action in the salve-mulls, naturally however, soon led to the study of the very opposite method of treating eczema, viz. by the pure drying-in remedies. If the fatty salves occasionally prove themselves unreliable, this has been shown, by a use of exclusively fatty salve-mulls, to be due merely to individual peculiarities.

Among drying-in vehicles for eczema remedies, glycerine jelly takes the first place.[1] This is mentioned here at length because it has hitherto been adopted much less than it deserves. What makes glycerine jelly so suitable for eczema is the combination of absolute permeability to the skin vapour, of slight but advantageous pressure on the parts beneath, of firm adhesion, utmost cleanliness, and relative cheapness in using large quantities.

Simple zinc jelly, or better still, zinc-ichthyol jelly (2 per cent. ammonia sulphich thyolate) comes in wherever salve-mull is inapplicable, as on the trunk of the body, wherever ointment cannot be borne, where fixation is desired without bandaging, &c., and where, on account of œdema, some pressure is necessary.

These jellies are especially useful in all acute eczemas—where formerly only powder was used. These affections—always vesicular, spreading, and accompanied by shooting pains and great tension—disappear, under the influence of a quickly painted-on film of zinc-ichthyol jelly, just as rapidly as they came.

For circumscribed favorably-situated patches, powder bags are almost equally efficacious, but for large areas of the body the jelly painting cannot be surpassed. We need not be afraid moreover of applying it thickly, even to the much swollen eyelids.

Should a specially increased pressure be desirable, there is no simpler or more pleasant method than to paint, over the whole part affected, a suitably prepared jelly, and then to

[1] 'Monatshefte,' 1883, No. 2.

apply a simple mull bandage, which can be painted over again with the jelly, and serve as a foundation for another bandage. In this manner, in addition to a soothing and anti-eczematous effect, any desired pressure can be permanently maintained by means of zinc jelly and mull bandage. It has been especially developed as a treatment of *congested* exanthems of the lower leg, due to stagnation—particularly ulcers. The jelly is painted on the skin around, leaving the sore free, and a double-headed bandage is so applied to the leg as to diminish the ulcer. If there are no sores present, the bandage serves to reduce the leg, which is usually eczematous.

The application of the zinc jelly necessitates its being previously melted in a water-bath, but this small trouble is amply compensated for in the comfort of the small, clean, and lasting dressing.

On the face the jelly application may be allowed simply to dry; in other parts it should be covered with some dry material. For this purpose, besides the mull bandages, common silk and tissue paper and cotton wool are suitable—the former on the trunk, neck, face, and central parts of the extremities; the latter on the points where movement would tear the paper.

In addition to their independent healing and mechanical uses, the jellies above named have proved themselves almost as useful as supplemental applications with salve and plaster-mulls. For instance, in a child with eczema of the head and face, to the head may be applied the zinc-ichthyol salve-mull, but in order not to interfere with suckling, the parts about the mouth and nose must be left free. These are to be painted over with zinc-ichthyol jelly, and covered with small pieces of tissue paper, as are likewise the edges of the salve-mull. The whole of the bandages may also be smeared over with the jelly, making a sort of firm mask. The jelly is also conveniently combined with plaster-mull, as we shall see later on, in connection with psoriasis.

For obvious reasons, very hot weather and profuse perspiration are contrary indications for the jelly treatment in eczema; the less soluble pastes are then preferable.

An eczema paste may be prepared by the poor, by boil-

ing in water, meal (100), and adding to the stiff paste, while hot, oxide of zinc (100), glycerine (50)—and, according to indications, sulphur (20), tar (50), or other substances. A very serviceable lead-paste, especially recommended for eczema of the hands and fingers because it resembles the colour of the skin, may be thus made: ℞ Amyli Oryzæ, 10; Lythargyri and Glycerini, āā 30; Aceti, 60; M. Coque ad 80. It also acts very well in painful eczema of the anus and scrotum leading to fissures.

Gum arabic and dextrine have proved useful, as soluble adhesive ingredients, which can be conveniently worked into pastes. These gum pastes are made by rubbing together mucilage, glycerine, and equal parts of dry powder: *e. g.* ℞ Zinci Ox., Amyli, Glycerini, Gummi Arabici, āā 20·0. M.

Among the dextrine pastes, the ichthyol paste may be particularly mentioned as a rapidly-drying treatment for all kinds of intertrigo, in slight eczemas of the face and hands which cannot stand grease, and also in universal eczemas. It may be thus prepared: ℞ Ammon. Sulpho-ichthyol., 1·0—3·0, Aquæ, Glycerinæ, Dextrini, āā 10·0. M. leni calore. This mixture forms a sort of liniment which quickly stiffens the skin, smarting for a moment on eroded surfaces, but soon stopping the itching and pain.

These pastes, like the jellies, are quite permeable to the skin moisture, and act, on drying, in a cooling way, like powder. But while the jellies can be made in large quantities and kept in stock, the pastes can only be prepared in small quantities and kept for a short time.

Intermediate between these pastes and the fatty ointments, are pastes made up with fatty substances, and they form on the skin a thick putty-like layer. Such are the "Bolus pastes," *e. g.* ℞ Boli Albæ, Ol. Lini, āā 30·0; Zinci Ox., Liq. Plumbi Subacet., āā 20·0. M.; and also the starch-vaseline pastes, *e. g.* ℞ Zinci Ox., Amyli Oryzæ, āā 10·0, Vaselini 20·0. M.

The fatty nature of these ointments is, as it were, advantageously corrected by the addition of drying powders.

In cases where an emollient is desirable, but not a pure fatty ointment, cold cream (Ung. refrigerans) may be suitable. The chief property of this is its constant cooling

effect, from the evaporation of the water, which it should contain in large amount: ℞ Ceriæ, Cetacei, āā 1·0; Ol. Amygdalæ, Aq. Rosarum, āā 10·0. M. f. cremor refrig. Common cocain is a substitute for this, as well as the well-known cooling mixture of lime water and linseed oil, with which pastes can also be prepared by the addition of oxide of zinc, &c.

While the external treatment of eczema has gained by the introduction of the above remedies, the ichthyol salts are the only new remedies which have enriched the internal therapeutics of the disease to any great extent. They possess an undeniably favorable effect, particularly in those obstinate recurrent cases which can be ascribed to a central nervous origin.

Valuable as these new methods may be for the majority of ordinary circumscribed eczemas, as well as for those forms which, on account of their unfavorable position (ear, nose, ankle, scrotum, &c.), have been hitherto amongst the most difficult to cure, and although, if wisely selected, they can at the outset cope with even universal eczemas, nevertheless, it must not be supposed that the old methods with fatty ointments have become altogether superfluous. The latter have only been relegated to their proper sphere, viz. the treatment of the various long-standing universal eczemas, especially when the dry skin needs lubricating; and for this purpose the ointments retain their dominant position.

The efficacy of the fatty ointments depends, on the one hand, on the easy permeability of the epidermis by fats, and on the other hand, the excess of grease obstructs the normal evaporation of water from the skin—gaining, therefore, for the absorption of remedies similarly favorable conditions, but in a less degree, as obtain under the impermeable plaster-mull. As Hack has shown, fats even increase absorption on granulating wounds, almost as much as water-proof bandages (Lister's protective).

Universal inunction is not, therefore, as lately stated, an unscientific method, but it is the easiest and relatively most pleasant way of ensuring a powerful influence on the whole cutaneous organ, and a constitional effect at the same time. We can, indeed, thus obtain a double effect—externally on

the skin itself, and internally through the blood which supplies the skin. Where vigorous action is indicated, we still, therefore, employ the universal inunction method.

With certain reservations, inunction is applicable to psoriasis as we see it to-day; for in this obstinate dermatosis the strongest action is generally not too much. The remedies recommended in this journal four years ago, chrysarobin and pyrogallol, are still the corner stones of our external treatment; and where a rapid and complete removal is desired of an extended and inveterate psoriasis, we must even now resort to a universal inunction with these drugs. The best plan is to combine the two, by rubbing the patient (meanwhile clothed in wool or flannel shirt, trousers, &c.), twice daily, from the feet to the shoulders with 10 per cent. chrysarobin ointment, and from the shoulders to the crown of the head with 10 per cent. pyrogallol ointment. It is advisable also to treat the hands of the patient with pyrogallol, and not with chrysarobin—to avoid conjunctivitis, by his inadvertently touching the eyes. To the genitals also, chrysarobin should not be applied; if they show psoriasis spots, they may be rubbed with pyrogallol ointment; if not, left alone. The most rapid colouring, irritating, and antipsoriasis action is observable on the flexor surfaces, especially of the joints, and on the genitals; and as soon as the irritation becomes unpleasant to the patient, these parts are to be excluded from the treatment by successively painting on zinc gelatine, and applying wool, so that the more obstinate places can steadily be treated further.

By means of these precautions, we generally succeed in obtaining a rapid, full, and uniform effect in four, eight, to twelve days (according to the amount of irritation produced), without chrysarobin conjunctivitis or pyrogallol discoloration of the urine necessitating intermission of the inunctions. After this maximum action is reached, the disintegrated horny layer is scraped off in a second cycle of treatment, in which either sublimate baths, 1 in 1000 (or ichthyol, 2 in 100), are used, or a course of ointments, or sulphur baths combined with the latter (tar and ichthyol ointments). When the skin regains its normal colour, the chrysarobin-pyrogallol inunctions should be resumed, as there are nearly

always some patches remaining, and then in a fourth cycle similar to the second, or the treatment may be more local.

The technical advances of the last few years have not been without influence on the local treatment of psoriasis. The combination of pyrogallol and chrysarobin with gelatine, at first welcomed with acclamation, has not quite justified expectations; the results did not compensate the intensity of its action. The introduction of the so-called "traumaticin"[1] as a solvent for chrysarobin, has been on the other hand most important. Comparative experiments as to the action of equally strong solutions of chrysarobin in traumaticin, collodion, and elasticin (india rubber in benzol), have shown that the traumaticin solution is the most efficacious application, and that it has two special advantages: first, it is the easiest to spread in very thin layers; and secondly, the chloroform is in itself a valuable antiparasitic. The more simple parasitic dermatoses (*e. g.* favus of the non-hairy skin) can be quickly cured by the application of traumaticin alone; and the more severe (*e. g.* herpes tonsurans) are best treated by medicaments dissolved in chloroform. If, therefore, a spreading psoriasis is to be treated locally, the patient being allowed to go about, the most suitable method, besides the anciently proved white-precipitate ointment and the alcoholic extract of tar, is to paint all spots every two days with a 5 per cent. chrysarobin-traumaticin solution. It will be frequently found, however, that around a beautifully healing patch, a wreath of young psoriasis papules will crop up without any inflammatory irritation zone, and the necessity may arise either to cease all external medication, or to fall back on the universal inunction cure.

A third way in which the efficacy of both of the new remedies has been verified is by means of the plaster-mull. This method of treatment, however, should be limited to those circumscribed forms of psoriasis which have shown themselves refractory to other means. The following precautions should always be taken: the psoriasis spots should be margined separately with zinc gelatine, or where the spots are close together, the whole may be included in one ring, and the pieces of plaster, cut rather larger than

[1] 'Vgl. Vierteljahrschr. f. Derm. u. Syph.,' 1883, p. 538.

the spots, but not so large as the zinc-gelatine frames, should be so applied as to partially overlap the former. The plaster-mull in the centre, and the zinc gelatine around, should then be smeared all over with zinc gelatine and covered with tissue paper. In eight to fourteen days the bandage may be removed, and even the most obstinate spot of psoriasis will be found to be nearly or quite cured. If it be not quite gone, the process may be repeated. By this means, the chrysarobin (or pyrogallol) will not hurt the skin, the application will retain its place, and new spots will not arise in the neighbourhood. There are inert skins which will bear thin plaster-mulls without any precautions, but these unfortunately are rare. The internal treatment of psoriasis has been advanced by the exhibition of large and surprisingly bold doses of iodide of potassium, 10 to 35 grammes (?) per diem ; and there is no doubt that by this means alone, rapid cures have been effected. This method can scarcely become general, but we may mention that in former times it was far more pushed as an auxiliary remedy in the treatment of psoriasis. It appears to be advisable to prescribe both iodide and arsenic in medium doses, separately, at different periods of the day, whereby better results are often obtained than by giving only the one drug. With children, if arsenic be not borne, ammonio sulphoichthyolate (0·5 to 1·0 grammes per diem), given in watery solution, has been found useful as an auxiliary. The ichthyol salt (2 grammes per diem) has also given good results with adults, either alone, or in union with iodide, but the facts concerning this are not yet made out.

We cannot, however, leave the subject of psoriasis without shortly indicating the prophylactic and curative measures which are at our disposal against the unpleasant bye effects of chrysarobin and pyrogallol. If the very painful chrysarobin conjunctivitis occurs, we have dressings with lead lotion, cooled with ice, cocain drops, and protective glasses for the photophobia, and as a prophylactic, we should during the whole treatment with chrysarobin—from its commencement till after its cessation—drop into the eyes, every three hours, a 2 per cent. solution of zinc sulphocarbolate (or a ½ per cent. solution of cocain). To avoid the toxic effect

of pyrogallol, a small dose of hydrochloric acid, every two hours, is advisable; and the larger the area of skin in contact with the pyrogallol the larger should be the dose of acid. If there be black urine, a small pulse, violent vomiting, &c., very large doses of the acid should be given day and night.[1] The acidulating of the blood acts as a direct antidote to the pyrogallol, the action of which only proceeding, as a rule, in an alkaline medium. Of course, in such a case, the external treatment must be suspended for a time, and the skin may be advantageously bathed with vinegar.

The treatment of acne has also made some advance in the last few years; and in the foreground stands now, as ever, the mechanical treatment. No medical man who wishes to obtain a quick and satisfactory result should neglect, at least at first, to scrape thoroughly, with a sharp spoon, every few days, the skin which is covered with pimples and comedones. This is to thin the epidermis in general, and to rub off the horny roofs of the follicles, and to open the pustules.

A damp compress, made of wool drawn out, allays the pain and bleeding at once. If many comedones be present, they can be easily removed by means of a special compressor, which has the advantage over the watch-key instruments that it can be pressed on not only perpendicularly, but also obliquely. The sharp side of the ring cuts open the corneous cover of the follicle, and the smooth side, by easy manipulation of the instrument between the finger and thumb, extracts the comedo in the direction of the hair sheath.

The scrapings can be replaced, as soon as obvious improvement has taken place, by rubbing every evening with fine marble dust; and this can be done by the patients themselves. A damp sponge is dipped in the dry powder, and the skin rubbed and evenly polished without pressure, until slight throbbing pain be felt. Then, instead of the usual sulphur paste, a stronger ichthyol paste is applied: ℞ Ammon. Sulpho-ichthyol, 3·0; Aq. Dest. Glycerini, Dextrini, āā 10·0. M. leni calore.

This is to be washed off in the morning with soap and warm

[1] We may order:—℞ Ac. Mur. Dil., Spt. Æther. Mur., āā 40; Aq., 350; Syr. Rubi, 50. M. S. 6 to 4, and later 2, tablespoonfuls every hour.

water, &c., weak sublimate solution used during the day: ℞ Aq. Rosarum, 200·0; Muc. Gummi Arab., Glycerini, āā 5·0; Zinci Oxid., 10·0; Hydrarg. Perchlor., 0·5. M. S. "To be shaken and applied after washing with warm water, and then, on drying, to be gently wiped off."

In all forms of acne which are complicated with rosacea, the prolonged internal use of ichthyol is also to be recommended; and, if in acne, the substitution of the ichthyol preparations for sulphur is to be called an advance—the eyes being never affected, and no sulphides bring deposited in the epidermis—it is of far more importance in rosacea. Thanks to the ichthyol preparations, the cure of this affection has been converted from a very troublesome, often thankless, and always lengthened process, to a very simple, gratifying, and comparatively short one. The puncture of the dilated vessels, which was formerly undispensable, is now required only for the very worst cases, and it can generally be omitted. Ichthyol internally is our chief remedy: ℞ Ammon. Sulphoichthyol, 5·0—10·0; Aq. Dest., 20·0. M. S. "15—30—50 drops, increasing the dose gradually, to be taken morning and evening in water." The aversion of patients to the smell can be overcome in all cases in two or three days, for the taste is not proportionately nasty, especially if the drops are well diluted with water, and taken at a gulp, on rising and retiring. Of course, we can prescribe pills of the necessary strength, but the watery solution is preferable. Ichthyol favorably influences not only the circulation anomalies of the nose, but also the commonly concomitant disturbances of other organs, *e. g.* hyperæmia and swelling of the mucous membrane of the nose and throat,[1] hyperæmia and chronic inflammation of the conjunctiva, congestion and chilblain erythema of the hands and feet, coldness of the extremities, hæmorrhoids, anomalies of menstruation, spasms from congestion of the pelvic organs,[2] &c., &c. The digestive organs are always improved by the internal use of ichthyol; the bowels are not forced but regulated, the appetite is generally improved, old gastro-intestinal catarrhs are cured, and the patients regain their elasticity. If there be palpitation

[1] Douches and gargles of 1 per cent. ichthyol are here serviceable.

[2] In this case rubbing in a 10 per cent. salve acts well.

and fulness in the head, Hallersch's acid, with or without digitalis, should be taken as well, and is by no means interfered with by the ichthyol. The latter should not be discontinued during the periods.

The use of cold water for the head in rosacea, is to be prohibited; bathing should only be with very hot water, and this should always be done after meals, and when the heat is increasing. The best soap to use is the superfatted ichthyol: indeed, slight forms of rosacea require no external remedies besides this soap. Further treatment depends upon whether the skin approaches to the acne type or to the eczema type. In the former we have, besides a more venous redness, an indolent habit, acne tubercles, pustules, comedones, and indurated epidermis; in the latter, more arterial injection and quicker change of blood, a weak skin inclined to scale, and often smarting and itching. The acne form requires strong measures, the best being those described above for acne, with ichthyol pastes at night, and sublimate solutions by day. The eczema form, if severe, should be treated with the remedies mentioned for eczema—lead paste, or zinc-ichthyol gelatine, or the powder bag by night, with powder after bathing during the day; or the above lotion may be prescribed without sublimate.

In turning now to lupus, we tread upon ground upon which it has been lately declared that we are ætiologically now as much clear on the subject, as in the case of the above-mentioned commoner dermatoses we are in the dark. The disproportion between our knowledge of the disease and the insufficiency of its therapeutics, has here been lately ventilated—as with tuberculosis generally; but we must neither fall into the errors of the too sanguine, who believe in everything ætiologically indicated—*e. g.* that because sublimate kills the spores of tubercle bacilli outside the body, it will also act well in the living tissues—nor allow ourselves to be influenced by pessimists, who, because the results do not correspond at once, give up the problem as insoluble. Recent experiments with the object of energetically attacking the tubercle bacilli in the skin, partly successful and partly unsuccessful, have taught us two facts with certainty.

In the first place, to destroy these micro-parasites in the skin, it is usually safer and simpler to modify those properties of the tissue which are necessary for the life of the parasite, than to attack the parasite directly, maintaining the full integrity of the tissue. It is especially necessary to get rid of the prodromal erythema which precedes the lupus tubercles. In this sense, every organ will have its certain antimycotic. Further, we must endeavour to find a remedy, or combination of remedies, which will, at the same time, impoverish the nourishing medium, and kill the parasite and its spores: this would really be a specific. The study of lupus must therefore be of the greatest importance for the therapeutics of tuberculosis in general: for here we can constantly control our discoveries with the eye. The cure of an ordinary case of lupus always commences best with a scraping—as thorough as possible—under an anæsthetic; and it has not been hitherto proved that this sanguinary method gives rise to any auto-infection; it certainly curtails enormously the course of treatment. After scraping, the margins and floor which contain bacilli should be treated energetically, either with lunar caustic, chloride of zinc, or sublimate; or, as these cause lasting pain, with a wool tampon dipped in a concentrated solution of pyrogallol, by which means the bleeding is stopped immediately. It must be remembered that in the neighbouring tissue, too firm to yield to the scoop, and along some of the dilated vessels, are lying undisturbed bacillary pioneers of lupus; and hence an energetic chemical treatment must now be adopted. The most agreeable method for the patient is to paint on, two or three times a day, the pure ichthyol salt—the burning which lasts for a short time being followed by a complete absence of pain. The redness promptly disappears, and the growth of new epidermis makes rapid progress: no bandage is necessary with it. A stronger effect is obtained by a 10 to 20 per cent. pyrogallol ointment; but the greatest depth action is attained by the use of plaster-mulls, particularly the arsenic-mercury, the pyrogallol, the salicylic, the salicylic-mercury, the salicylic-iodoform, the iodoform, the iodide of lead, and the mercury-carbolic plaster-mull. These are directly applied to the surface of the wound.

The addition of sublimate to these remedies has been proved to be painful, and not necessary—the results not being better. We must now bear in mind the dilated vessels, endeavour to get the whole skin to contract, and to lessen the supply of oxygen to the bacilli.

If this method of treatment prove impracticable, it is then best to thin the horny layer as much as possible with a strong salicylic plaster-mull, and afterwards to apply the plasters just mentioned, separately, or in turn, until all the tubercles are healed.

The scarification of lupus, although of good effect by the destruction of the vessels, has rightly fallen into disrepute, because, operating in the dark, auto-infection can easily take place. For the same reason, simple punctures of the edges are not to be recommended; but in their place, puncture injections have been lately introduced as a well justified operation; as the whole depth is bathed by a concentrated medicament, the possibility of auto-infection is excluded. The accompanying sketch[1] shows such an injector. By gentle pressure of the forefinger on the upper elastic membrane, we are enabled to introduce the medicament in drops close to the point of the puncture knife; and in this way large surfaces of lupus can be treated mechanically and chemically at the same time. As injection fluids, the following can be recommended:—50 per cent. ichthyol solution, with or without tincture of iodine, a 10 per cent. solution of pyrogallol, a 2 to 5 per cent. solution of potash, or a 5 per cent. solution of creasote, &c. Sublimate solutions are unfortunately inapplicable, as they destroy the instrument too soon. These puncture injections are advisable as the treatment for solitary lupus tubercles, for they can be applied without narcotics.

This review of some of the principal dermatoses may terminate with furunculosis and erysipelas, the treatment of which, even before their ætiology was clearly known, has been much more successful under the dermatologist than under the general surgeon. An experience of five years has shown that all those suppurations which we know under the names of "furuncles," "carbuncles," "abscesses," "panarites," and

[1] [In the original paper.]

"phlegmon,"—and which are traceable to infection from certain kinds of cocci—can frequently be cut short if treated early, always running a more benign and milder course, with lessened suppuration, and needing incision in but rare cases. The universal remedy for all these suppurations is the mercury-carbolic plaster-mull; and how it acts depends upon the stage when it is used. Applied to a commencing boil or on a just emerging panuritium, over a large surface, it causes a disappearance with only a slight remaining redness. Laid on later, it limits the suppuration to the central most infected part, and quickly gives rise here to a spontaneous and painless rupture—the aperture, which is much smaller than could be made by incision, soon closing again under the plaster. In larger suppurations which are nearly ripe, the application of the plaster-mull at least shortens the time of bursting, or if an incision has been made—which should be made as small as possible—the time of healing is considerably quickened. The pain, moreover, is greatly alleviated. The necrotic sloughs are frequently quite absent under this treatment, and in carbuncles they are much smaller than when left to themselves. The favourite aperture in the centre of the plaster is to be omitted with these plaster-mulls—for it would defeat their main feature—viz. water-proofness. Should any considerable amount of pus collect between the skin and the plaster-mull, it may be washed off after raising the latter, and the plaster-mull, or a new piece, may be replaced. Where the position of the skin permits, and if it be convenient to the patient, an ordinary linseed poultice over the plaster is very advantageous. In panuritia and furuncles of the hands and feet, especially where the skin is already broken, soaking in an alkaline bath is useful (with soft soap, potash, or soda). Of course, no physician would hesitate to open at once a highly-developed suppuration about to burst, and very painful; but, even then, subsequent treatment with the plaster-mull is the most agreeable for the patient, changing the large opening to an inconsiderable fissure, and improving the subsequent scar. From the dermatological standpoint, we must decidedly protest against the unnecessary torture of constantly cutting recurring boils, and also against the painful and, as far as the patient is concerned, useless

—although classical—cross-cutting of carbuncles. A furunculous patient who has once experienced the good effects of the plaster will anyhow lose the taste for the knife; as soon as all his boils are properly covered with the plaster-mull, their subsequent development will stop. Carbuncles may be advantageously bathed with solution of ammonia, or of alkali, before each application of a new plaster. In cases where recovery cannot take place without some suppuration, it is better to leave undisturbed the plaster-mull and the skin: by covering the whole region with plaster, a deep-lying necrotic bone splinter, whose course was quite uncertain, has frequently come to the surface, painlessly and gradually, at an unexpected spot.

Where hair makes the use of the plaster impracticable, *e. g.* for furuncles after eczema capitis, or in frequently recurring boils of the axillæ, a rapid cure can be attained by the application, twice daily, of a 10 per cent. ichthyol ointment—which is also a very good substitute for the plaster in disseminated furunculosis. The best internal remedy for cutting short a suppuration is calcium sulphide (about 0·01 grm. ter die), administered as "small-intestine pills."

The reducing remedies, already so often mentioned (pyrogallol, resorcin, and ichthyol salts), have lately been successfully used for erysipelas in place of turpentine and iodine; and their action is quicker and generally more painless. They may be smeared on as ointments—the ichthyol salt in strength of 20 to 50 per cent., resorcin in 10 to 20 per cent., or pyrogallol, 5 per cent.; or they may be applied in salve-mulls. From its freedom from smell, and absence of all danger of intoxication, resorcin is to be preferred in well-circumscribed erysipelas; but in the ambulatory variety it is better to apply ichthyol ointment to the whole skin. In every case desquamation takes place, the horny layer becoming brown and shrivelled, and bringing the process to an end. We may also remember the equally pleasant silicate of potash ("water-glass"), a simple paste which acts partly by pressure and partly by setting free its alkali, and which has wrongly fallen into oblivion.

Having mentioned only some of the most important points concerning modern dermatotherapy, we may well say on

looking back that the last few years have not been barren in regard to the practical side of our special branch. Our goal has been a reform of the dermatological armamentarium; and this is by no means yet complete. Some most important work still awaits perfection; *e. g.* the preparation of medicinal soaps and of medicamental pencils and pigments—understanding by these, remedies to be painted on the skin and leaving a permanent impression. The medicated ether-spray also deserves a crucial trial on a large scale, for in certain cases it has worked wonders.

Lastly, the endermatic and subcutaneous methods require new trials in dermatology. The time, indeed, is approaching when general researches must be carried out in this direction, and it will then be only a matter of working them out for special drugs and special dermatoses. The coming three years will mean more for dermatology than laying down general rules for its therapeutics, of which the foundation walls already stand.

From the seed sown by Koch, it is to be hoped that work on the etiology of diseases of the skin will spring up, which will soon clear up the question lately raised by Aussitz as to the entity of skin diseases, and at last release us from the system of Hebra, which has become as a strait-jacket.

For this, younger forces are required, trained in new methods; and this retrospect may therefore be concluded with an appeal to the young physicians of Germany to devote themselves with zeal to this newly revived and promising branch of dermatology.

Archives, May, 1885.

# CONTRIBUTIONS TO OUR KNOWLEDGE OF LANOLIN.

In Dr. Unna's opinion it is chiefly the chemical inertia of lanolin, and its special physical properties, that will give it a permanent and high place in the pharmacopœia. He cannot confirm the presence of lanolin in the human skin; cholesterin, however, occurs abundantly.

*Lanolin and Plaster-mulls.*—The author traces the improvements in the manufacture of plaster-mulls, and their development from the original salve-mulls, and remarks that the reason why the German preparations are so much superior to others is that they are made under the guidance of a dermatologist who is alive to the advances of technical science. The gutta-percha plaster-mulls which were ultimately made could hardly be surpassed, being impermeable to water, more adhesive, and having a deeper action. At first benzoated lard or tallow was used as a basis, and vaseline for easily decomposed drugs, or wax for very volatile substances. The use of oleate by Beiersdorf was a distinct advance, as being more adhesive, non-irritant, and antieczematic. Since 1885 anhydrous lanolin has gradually replaced all these, being very tough, adhesive, stable, and absorbent for large quantities of water. Benzoated lard, however, is still used as a basis for carbolic acid, and wax for mercury and creasote. From the inertness of the new vehicle, which should then be quite dehydrated by heat, even such substances as pyrogallol and nitrate of silver can now be incorporated in plaster-mulls.

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(150 per cent.) are enough. Experiments to determine the best proportion of the ingredients showed that—

(1) Lanolin, 10+Lard, 20, could be saturated with 70 parts of water.
(2) Lanolin, 15+Lard, 15, „ „ 90 „
(3) Lanolin, 20+Lard, 10, „ „ 110 „

Saturation is reached when the mass no longer sticks to the spatula, and when drops of water can be pressed out, and this will depend upon various conditions of temperature, &c. The above figures prove that with the increase of lanolin there is not a proportional absorption of water, and on applying the mixture to the skin it was found that No. 1 was stable and suitable for inunction, while with Nos. 2 and 3 so much water was expelled that inunction could not be properly completed. Hence it is best to be satisfied with a proportion of water to fat of 2½ to 1, and the lanolin should not exceed half the amount of the benzoated lard.

The consistence of these compounds is less firm than that of the ordinary cooling ointments, and approximates more to that of ordinary cream—a substance which, in the author's opinion, might be more used in dermatological practice as a cooling application, from its containing so much water for evaporation, and enough fat to keep the skin subsequently soft.

As previously pointed out, there are two classes of refrigerating ointments, differing in consistence and amount of water contained. The first are unctuous, for rubbing in on limited areas of skin, and may be considered as ordinary cooling ointments. The second are more saturated with water, and creamy, and can be applied in large quantities over erythematous, burning, or itching areas. These may be called "cream ointments," and are best prepared as above. In practice, on account of varying conditions, such as climate, and the length of time of trituration required for saturation, &c., the amount of water may be kept considerably below the maximum. As a rule, 200 per cent. of water can be easily and certainly incorporated. The best relative proportions of the ingredients for a "refrigerating ointment" are—lanolin 10 parts, glycerine fat 20, and water 30; and for a "cream ointment"—lanolin 10, glycerine fat 20, and water 60 parts. In all cases, of course, anhydrous lanolin should

be used. The choice of fat to be used will depend upon conditions of temperature, &c.; and in place of the water, watery solutions of cooling drugs may be added, such as Liq. Plumbi Subacet. and lime water, or solutions of substances which may assist by producing anæmia, like ichthyol, resorcin, and tannin.

The following are useful formulæ, with their chief indications:

| | | *Indications.* |
|---|---|---|
| *Ung. Refrigerans*— | | |
| Lanolin Anhyd. | 10 | The ordinary indications of "cold cream." |
| Adeps Benz. | 20 | |
| Aq. Rosæ | 30 | |
| *Ung. Refrig. Aquæ Calcis*— | | |
| Lanolin Anhyd. | 10 | Burns, and as ointment basis in hyperæmias, rosacea, acne. |
| Adeps Benz. | 20 | |
| Aq. Calcis | 30 | |
| *Ung. Refrig. Plumbi Subacet*— | | |
| Lanolin Anhyd. | 10 | The indications of Goulard's ointment, eczema, lupus, lupus erythematosus. |
| Adeps Benz. | 20 | |
| Liq. Plumbi Subacet. | 30 | |

The basic substances contained in the last two are especially useful for reducing hyperæmia, as is a cooling ointment containing carbonate of soda. Although alkali soap has a similar action, it is, like the solvents for fats, ether, and chloroform, incompatible with these ointments.

When fats are badly borne, a cooling zinc ointment can be thus made: Lanolin, 10; Ung. Zinci Benz., 20; Aq. Rosæ, 30; and a refrigerating pomade—Lanolin, 10; Ung. Pomadini, 20; Aq. dest., 30. For a hot erythematous scalp the water may be replaced by Aq. Calcis.

The cream ointments cannot be modified to the same extent; the chief are—

*Cremor Refrigerans*—Lanolini, 10; Adeps, 20; Aq. Rosæ, 60;

*Cremor Refrig. Aquæ Calcis*—Lanolin, 10; Adeps, 20; Aq. Calcis, 60; and

*Cremor Refrig. Aquæ Calcis*—Lanolin, 10; Adeps, 20; Liq. Plumbi Subacet., 60.

As they readily undergo change, they should be freshly prepared and used quickly and abundantly. Even the refrigerating ointments cannot be kept indefinitely.

# MEDICATED SUPERFATTED POTASH-SOAPS (OINTMENT SOAPS).[1]

MEDICATED soaps may be classified as hard soda-, or soft potash-soaps. After many attempts the author succeeded two years ago in obtaining the former, so prepared as to meet the requirements of the dermatologist. For their manufacture, which can only be on a large scale, the combined experience is necessary of a dermatologist, a pharmacist, and a soap-boiler, free from the usual prejudices of his class. The preparation of soft soaps, on the other hand, can be undertaken by any pharmacist, without fear of their deteriorating in quality or homogeneity, and on a small scale, with varying ingredients as may be indicated.

Although non-medicated soft-soap has long been used with effect by dermatologists in chronic inflammatory conditions, it has not been until now employed as a vehicle for active therapeutical agents. Since Oberländer, in 1883, recommended it as a basis for the inunction of mercury, the author has largely practised the method; and he was stimulated in this by the preparation by Dr. Mielck of an efficient soft-soap preparation as a substitute for the iodide of potassium ointment of the pharmacopœia. The success of the ichthyolated hard-soap also suggested the preparation of a potash-soap compound, which might be stronger in absorbent and antihyperæmic action. Here, too, the result surpassed expectation. His experience in the use of four medicated

[1] "Medicinische überfettete Kaliseifen (Salbenseifen)," 'Monatsh. für prakt. Derm.,' v Bd., 1886. p. 348.

soft soaps containing mercury, iodine, ichthyol, and ichthyol-tar has been so encouraging that he strongly recommends them and other preparations of the kind to his colleagues.

In the manufacture of such compounds certain principles should be followed. First, it is of importance to mix the soap with an excess of unsaponified fat, for, as it has been well known since Capesser's active inunctions, the epidermis cannot otherwise bear the continued applications. A neutral soft-soap should be first obtained, and then the fat added, in quantity and quality varying with the active drug prescribed.

As these soft-soaps take an intermediate position between soaps and ointments, they may be called "Ointment-soaps" (*Sapo unguinosus*). The ordinary potash-soap, prepared from oil, is too soft for the purpose. One prepared, however, from lard, as suggested by Dr. Mielck, answers all requirements, and this, with the addition of 5 per cent. of benzoated lard, forms the basis of the ointment soaps.

Like the hard soaps they may be employed in several ways. The most powerful and irritating effect is obtained by leaving a strong lather to dry on the skin; but a less irritating method is to wipe off the lather with a dry cloth. Ordinary washing with the ointment soap is of no avail, unless perhaps repeated many times daily; but a powerful action may be ensured by rubbing in the lather for five, ten, or fifteen minutes at a time with cotton-wool or with a brush dipped in hot water, and then washing off.

The author generally fixes the excess of fat at 5 per cent., but a larger quantity, or other dilutents (glycerine, vaseline, lanolin), may be added as indicated. With larger amounts of fat the soap ointment gradually loses its soap character, and we may have merely a soap-containing ointment like lanolin.

Mercurial ointment soap (*Sapo cinereus unguinosus*) differs from that of Oberländer in being superfatted. It is prepared by mixing one part of mercury with one-sixth part of *Ung. cinereum*, and then adding two parts of soft-soap obtained as above. The best way of using it is to rub it uniformly over the affected area, then to lather it for some time with hot water, and finally leave it to dry on the skin. If the

latter be indolent and non-absorbent, a stiff brush should be used; but ordinarily a pad of cotton-wool or the patient's own hand suffices.

The quantity used should be regulated to the size of the area for inunction; and to the medical man the only criteria, as regards the intensity and duration of the treatment, are, on the one hand, the disappearance of the symptoms of the disease, and, on the other, the appearance of undesirable effects of the remedy.

The chief advantages of this ointment soap over the ordinary blue ointment for mercurial inunction consists, first, in being able to introduce a larger amount of the drug into the system, especially in the case of certain individuals with an abnormally fatty skin, and, secondly, in its easy application to any part of the body and in any desired quantity. Its greater cleanliness and economy are also important. On the average 30 grammes of this ointment soap are equivalent to 40 grammes of the old mercurial ointment. Patients, moreover, invariably prefer it, from its greater cleanliness, more comfortable sensation of the dry skin, and less odour. It is undoubtedly preferable also for the local treatment of enlarged glands.

Iodide of potassium ointment soap (*Sapo kalii iodati unguinosus*). The inertness of the pharmacopœial preparation is well known, hence the introduction of this compound will be welcomed, as there is no decomposition of the iodide until it is rubbed on the skin. Dr. Mielck, who prepared it, has written upon the subject himself. The formula is: Ointment-soap 9 parts, iodide of potassium 1 part, and water a very little.

Ichthyol ointment soap (*Sapo unguinosus ichthyolatus*) is more active than the ichthyolated hard soap, whose indications (chiefly rosacea) the author has elsewhere fully considered, and hence it has a wider sphere. Intertrigo reacts promptly to it, if energetically applied by lathering and wiping off dry; also various forms of furunculosis, acne and rosacea; but here we must regulate the strength and method of application according to the indolent or irritable state of the skin. In seborrhœic diseases, from simple pityriasis capitis and dry seborrhœa to universal seborrhœic eczema,

this ointment soap should be lathered on for a considerable time with a brush, and left to dry. It is also excellent for acute eruptions in the course of chronic eczema, for urticaria and lichen urticatus, circumscribed chronic eczema, before applying ointments or plaster-mulls for chilblains, for the host of superficial rheumatic affections; in short, in all cases where the action of ichthyol is as desirable as that of soft soap. The strength may vary according to the case: Ointment-soap 10 parts, Ammon. Sulpho-ichthyol. ½ to 5 parts.

Ichthyolated tar ointment soap (*Sapo unguinosus piceo-ichthyolatus*) which contains: Ointment-soap 7 parts, Ol. Cadini 2 parts, Ammon. Sulpho-ichthyol 1 part, is a modification of the type introduced by Wilkinson in his tar-sulphur-chalk soap ointment. The ichthyol replacing the sulphur permits the concurrent use of lead or mercury, and the larger proportion of the ointment-soap does the work of the chalk in neutralising the acid constituents of the tar. This combination is especially useful in obstinate circumscribed infiltrations, like *Sycosis vulgaris*, and in certain forms of eczema. It has the advantage of being useable during the day, even for the face, without being noticed, by lathering with much water and then washing off.

ON

# THE USE OF ICHTHYOL IN INTERNAL DISEASES.

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In answer to a question from a correspondent, the author gives his experience in the 'Monatshefte für praktische Dermatologie,' 1889, No. 12.

Although he had used ichthyol continuously for seven years, for the past five years it was only in those internal and constitutional affections which accompanied diseases of the skin. The indications for its use, however, he has found numerous, and he considers that his observations may serve as hints to physicians.

The diseases treated he divides into (1) Diseases of single organs or systems, and (2) General diseases.

In the first class he begins with affections of the peripheral circulatory system. In many cases of seborrhœa of the head and seborrhœic eczema of the face, in women, the symptoms finally depend on abnormal peripheral distribution of blood. There may be one or more of the following symptoms:—A waxy white or yellow tint, anæmic lips and conjunctivæ, oily seborrhœa of the face, recurrent hemicrania, pain in the back and loins, menstruation small or passing into amenorrhœa, habitual constipation, anorexia, abnormal sensations during digestion, palpitations, especially on exertion, lassitude, drowsiness, and giddiness. In such cases ichthyol does well, and it may be continued for months or

years ; not only does it make the skin a less favorable soil for seborrhœic eczemas, but it makes new beings of the patients, and "does them so much good" that they will, on their own account, keep on with the remedy for years.

Another type of general disturbance of peripheral circulation is found in elderly men predisposed to rosacea, who lead sedentary lives and are fond of alcohol. They are often short and thick-set and tend to obesity, with perhaps enlargement of the liver and chronic hyperæmias and catarrhs of the pharynx and bronchiæ, &c. Here, too, ichthyol, given for the rosacea, has a happy effect on the other hyperæmias and catarrhs.

Next in importance comes a large number of diseases of the digestive tract. Under the internal administration of ichthyol—and this observation has been abundantly confirme,—cases of old catarrhs of the stomach and intestines, accompanied by anorexia, furred tongue, irregular bowels, tympanitis, wasting and mental depression, are often cured completely, although they have not yielded to the ordinary drugs. It is desirable that specialists, in diseases of the stomach and intestines, who do not seem hitherto to have availed themselves of ichthyol, should accurately give us the indications for its use in such cases. Two points may be specially alluded to : (1) the improvement in the general health was noticed sooner than the catarrhs and circulation disturbances at the root of the matter can be looked upon as cured ; and (2) that in some cases a favorable action was observed on cholelithiasis, so much so that the yearly journey to Carlsbad became superfluous.

The third class includes diseases of the respiratory organs. The topical action of ichthyol and its inhalation are disregarded, but its internal use has been successful in several cases of bronchial asthma. In three cases, in which the attacks could only be controlled by large doses of iodide of potassium, their severity and frequency were much reduced, the bronchiolitis and cyanosis decreased, and the general health and power of resisting the effects of weather improved. In one, which had been under treatment for four years, a permanent cure was effected. An important advantage of ichthyol is that, unlike the iodide, its use can be continued

for years. In severe cases it is well to combine the two drugs, at least during the attacks.

Ichthyol is also advantageous in the bronchial catarrh of old people, especially when accompanied by asthmatic attacks of dyspnœa. This affection is not uncommon in old patients with universal chronic eczema, and the author has several times observed in them a diminution of the catarrh, expectoration, and dyspnœa, under the ichthyol treatment.

In the fourth set of cases may be placed diseases of the uropoietic system. It is hoped that Tülzer, who has had good results, will give us from his rich material more accurate indications for its use than can the author, whose cases have been chiefly of cystitis following gonorrhœa. In these he has seen no effect from ichthyol internally given, but in his former practice, in 1881, an elderly gentleman with nephrolithiasis, pain in the kidney region, and digestive troubles, derived marked benefit from ichthyol, which he had continued to take regularly on his own account for four years. He was seen lately as a healthier and stronger man, with his kidney and gastric troubles totally gone. The use of ichthyol for so long a time is by no means unique; patients have taken it for still longer periods, and have been most grateful for the cure or alleviation of their chronic troubles.

Among general ailments, the first place must be given to rheumatism in its various forms—from simple muscular rheumatism to *arthritis deformans*. The good effect of ichthyol in diminishing the pain and reducing the temperature in acute rheumatism, as well as its favorable influence on the disease in general, have been tested and confirmed by so many competent observers since the author's communication in 1883,[1] that further allusion to this disease is here unnecessary.

The second place may be awarded to chronic and acute alcoholism, in which little has been heard, so far, of the treatment by ichthyol. The effect of a single large dose (1 to 2 grammes) was so favorable on the circulatory disturbances in one case, that the author has employed it largely

[1] "Das Ichthyol bei inneren Krankheiten," 'Deutsche med. Zeitung,' 1883, p. 217.

where the patients were addicted to the excessive use of alcohol. The sluggishness of the peripheral circulation, and the tremor of the hands and tongue vanish and the appetite for solid food increases, while a dislike for drink is developed. The patients, indeed, are weaned from their habit; and this hint may be taken by the managers of asylums for dpsomaniacs.

There have been several encouraging cases of its use in diabetes and true chlorosis, where its undoubtedly favourable influence on the concomitant digestive disturbances may have much to do with the improvement.

The author has had larger experience of ichthyol in the case of cachexias in general. In many cases of hopeless tuberculosis, carcinoma, leprosy, and in debility caused by tertiary syphilis, the general health has been raised to a higher level.

Improvement in the appetite, muscular power, and general appearance, due to a strengthening of the peripheral circulation, is soon noticed by the patients themselves; and they willingly take the drug in the hope that it may cure the disease at the bottom of their troubles. Is the effect due only to a symptomatic influence on the circulation, to an improvement in the general circulation through increasing the appetite, or to an antidotal action to the ptomaines on the tissues of the body? This question, which we cannot answer to-day, will probably soon be determined by physiological and therapeutical experiments. At any rate, even now, ichthyol must be classed among our most valuable drugs for the treatment of chronic infective diseases leading to cachexia.

Every medical man should acquaint himself with its properties; and the more he studies its indications, the more confident will he feel in its application.

# ON THE TREATMENT

OF

# TRICHOPHYTON CAPITIS.[1]

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The question of Trichophyton treatment was put forward for discussion at the Paris International Congress; and with the burning interest which this question possesses, especially for London and Paris, the discussion promised to be very instructive for us Germans. In the polyclinique of every London hospital are treated yearly many hundreds of children, the subjects of trichophyton; and similar multitudes are seen at the St. Louis Hospital in Paris. What experience is here accumulated, and what difficulties must the treatment present—reading as we do, especially in the London journals, that new remedies are constantly being tried, and, for the most part, soon laid aside!

The result of the Paris discussion was, for unprejudiced listeners, that we are still in the midst of the experimental stage of the treatment of this unpleasant disease of school children. Neither in respect of the cure generally, nor in regard to the duration, method, or time of treatment, was there any agreement whatever. On account of my very small experience of the subject, I had decided not to enter into the discussion, but was drawn into it against my will by my honoured friend Besnier. Now, however, I think I may confidently come forward with my small experience, and at the

[1] An address given in the section of Dermatology and Syphilography at the Sixty-second Meeting of the German Naturalists and Physicians in Heidelberg, 1889.

same time answer Besnier's question. If my material has been scanty, my results, at any rate, have been uniformly favorable during the last three or four years.

Proceeding from the generally acknowledged fact, that we possess in chrysarobin the most efficacious remedy against most of the mycoses of the skin, I have endeavoured to use it for the trichophyton of children's heads. I may well conclude, from the surprising circumstance that it has not been so employed by others, that most dermotologists rightly fear its influence on the neighbouring eyes; and I have tried to eliminate, in a simple manner, this very annoying contingency. First of all, the whole scalp must be cropped short (not shaved)—even though only a few bald spots be present; for, as it soon becomes apparent under the treatment, there are always more hairs attacked than we may at first sight imagine. The same plan must of course be adopted if there be no bald spots, but only scattered stumps. The whole forehead of the child, the temples, the ears, and naked parts, are then covered with strips of zinc gelatine; and after this has been done, the scalp within the zinc gelatine margin is carefully painted over with a strong chrysarobin ointment, *e. g.* my Ung. Chrysarobin co. (Chrysarobin 5, Ac. salicyl. 2, Ichthyol 5, and Ung. Simpl. 100) or any other ointment containing from 5 to 10 per cent. of chrysarobin. The hairy part of the head is then covered with some waterproof material (waxed linen, gutta-percha tissue, &c.), the edge lapping over the marginal strips and gummed down with zinc gelatine, then bound with an adhesive mull binder; and, lastly, a well-fitting flannel or wax-cloth cap is tightly fixed over everything with strings.

Once in twenty-four hours the cap is removed, the waterproof material cut along on one side and reflected, and the head washed, dried, and covered again with fresh ointment: the slit in the material is then closed with fresh mull strips, and the cap replaced. If this proceeding be really carefully carried out, on the fourth day—when the first chrysarobin cycle is terminated—only the upper edge of the zinc gelatine strips should be stained yellow from chrysarobin. Every spot of the latter is at once to be seen on the white ground of the border strips, so that an unobserved contact with the eye is

impossible. Should there be any discoloration of the lower part of the marginal strips or of the neighbourhood near the eyes, it should be washed off, and smeared over again with zinc gelatine.

With this bandage we can allow children to play about quite harmlessly; they may sleep in it, and even go to school, being not contagious nor dangerous either to themselves or others.

On the fourth day, when the cap is removed, the chrysarobin ointment is washed off, and replaced by a 5 per cent. ichthyol ointment, which is to be used for the remaining three days of the week—in order to allay the irritation produced by the chrysarobin, to make the horny layer fall off quickly, and to bring the skin back to its original colour. This application may be replaced by a 5 per cent. ichthyol solution, or, not so well, by a 5 per cent. sulphur ointment —also to be applied every day for three days.

Now, only at the end of the first week can we wash off without danger the zinc gelatine strips at the back, and cleanse the whole head properly with oil and soap. The diseased parts are now very apparent from their white colour contrasting with the healthy scalp around, and they frequently astonish us from their unexpected number. From all these places some stumps (about 20 altogether) are epilated, in order accurately to observe the condition of the fungus.

After this the second cycle is commenced, and this lasts also for a week, and runs the same course as the first. At its termination, again 20 stumps are drawn out to confirm the improvement.

A third and a fourth cycle, following, generally conclude the treatment. I have not found it necessary to follow on with a fifth. The total length of time required for my treatment amounts, therefore, to four weeks. Possibly the very old and severe cases of the London hospitals would need a five, or at most, a six weeks' course. This result, at any rate, is immeasurably different from that obtained by the best London dermatologists, who are accustomed to estimate the treatment of medium cases always by months, and who can even speak of cases under treatment for years.

My observations, moreover, are much more consoling than those of Besnier, who, indeed, quite doubts a real cure by the aid of Art.

It is in consequence of the results of my cultivations of the fungus during the treatment, that I venture to make such a confident statement as to the possibility of so quick and certain a cure for Trichophytia. It is a matter of very little trouble to pull out a few suspicious hairs before treatment, and at the end of each cycle, and to place them to grow in agar-gelatine tubes. Even before the end of the next week, we are in a position to determine exactly, according to the result of the cultivations, whether any advance has been made toward recovery. As a matter of fact, if the above method of treatment be adopted, there can be seen an advance, from week to week, up to the complete sterility of the hairs of the fourth sowing. Dr. von Schlen, who has lately made these experiments, will go more into details at the end of my lecture.

To prove the results of treatment by cultivations from hair-stumps is so simple a matter, and so convincing, that the method is to be strongly recommended to every dermatologist, even for his own satisfaction. It is nowadays, indeed, indispensable for the scientific comparison of the different methods of cure of the disease. I have seen no relapses after this chrysarobin method. The usual contra-indications will scarcely be present, unless perhaps the excess of material at the London institutions may be so regarded. The only one I know of—and this is not absolute—is where a skin possesses such sensitiveness to chrysarobin that a single application produces erythema and œdema. As a rule, the scalp reacts indolently to it; but exceptionally, after using the ointment a few times, œdema may appear with pustules. This can be treated with 3 per cent. and then 1 per cent. ointment solution, or else with a weaker chrysarobin and salve ointment. The final result, however, is equally good; indeed, by skilful management of the irritation caused by chrysarobin, these cases are cured in a shorter time than others.

I hope that our London and Paris colleagues will be able to obtain equally good results from this method.

# ADVANCES IN THE ANATOMY OF THE SKIN.

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## Nerve-endings in Human Skin.[1]

About a year before this paper was written the author was induced, by some work of Pfitzner's on frogs and newts, to study the nerve-endings in human skin. He treated some sections of human prepuce, from which the fat had been removed, with a weak solution of osmic acid, and found that each prickle-cell was provided with two non-medullated nerve-fibres which, without communicating with each other, ended close beside the nucleus. In preparations, from which the fat has been removed, one can see that medullated nerve-fibres spring from the superficial and sub-epithelial plexuses which end in the touch-corpuscles, and that other shorter medullated fibres break up into delicate medullated threads, some of which end in small terminal swellings beneath the epithelial layer, while they end in the endothelium of the blood-vessels, and especially in the capillaries of the papillæ.

The delicate non-medullated plexus, which lies between the superficial medullated network and the epithelial layer, gives off numerous branches to the epithelium, which run in the spaces between the prickle-cells. These fibres give off lateral branches to the prickle-cells, which, after piercing the protoplasm of the cells, terminate between it and the nucleus in rounded or oval knobs. They never enter the

[1] "Die Nervendijung in des Menschlichen Haut.," 'Monatsh. f. prakt. Derm.,' Bd. i, 1882, No. 8.

nucleus itself. These end-bulbs do not seem to be quite of the same material as the fibres, for they react differently to reagents. The author has shown the existence of these nerve-endings in the whole prickle-cell area, extending as far as the granular layer, but they do not occur in the horny layer. He finds them along the whole course of the sweat-glands, and in the whole extent of the root-sheaths of hairs.

He has observed them in adults as well as in new-born children. These end-bulbs also occur between the prickle-cells; but the intra-cellular arrangement is more usual.

The most remarkable feature about these nerve-endings is that they always occur in pairs. They are not merely passive enclosures between the epithelial cells, but they enter these themselves, and so stamp the whole superficial skin as an organ in the play of the nervous system.

## The Fibrillar Structure of the Prickle-cells, and their Communicating Processes.[1]

The author reviews the various recent observations relating to the prickle-cells and their processes. In 1879 Ranvier stated that the so-called "prickles" of Max Schultze did not exist as such, but that they are the broken fragments of protoplasmic connecting threads, which can be seen *in situ*; and he also maintained that the little mid-swelling of the filament is not, as Bizzozero thought, due to the soldering together of the prickles, but that it is rather of the nature of an elastic knot, which permits the separation of the cells, within certain limits, without rupture of the connecting link. He stated that the swelling only exists on the shorter threads and not on the longer ones which connect cells further apart. Three years later, by a special method of staining, Ranvier observed a close meshwork of fine threads around the nucleus of the cell, with filaments from the network crossing over to neighbouring cells through the connecting processes, of which they only occupy half the diameter. He identified them with the thread-like

[1] 'Die feinere Struktur der Stachelzellen und ihre Verbindungs-Apparate,' 'Monatsh. f. prakt. Derm.,' Bd. vii, 1888, No. 17.

constituents of the cell-substance, as found by other histologists (Kupffer, Fleming), but did not regard them, like Kupffer, as "protoplasmic" in contradistinction to "paraplasmic" structures. Cajal, in 1886, on the whole, corroborated Ranvier's views, except in certain details. He distinguishes in lip-cancer two kinds of prickle-cells, a smaller, opaque and granular, and a larger, transparent and fibrous variety. In both the threads form a network around the nucleus (but leaving in the former a transparent fibre-free zone next to the nucleus), and pass to the neighbouring cells through the processes. On their way across, he, like Ranvier, finds the threads thicker, and admits an outer layer, which, however, he believes to be cuticular and not protoplasmic; for protoplasm is fluid, while the connecting link is stiff and more refractive. He has an original explanation for the spindle-like swelling in the middle, viz. that the cuticle is often torn and rolled around, and thus giving the appearance of a knot. In the transparent cells, which are found in the neighbourhood of the nests, the numerous fibrillæ are thoroughly refractive and running parallel closely together, and often pass directly from one cell to another. They resemble, on the whole, the fibrillar cornifying cells of the hair-papilla and Henle's sheath, the threads being thicker, more parallel, and more distinct.

Bizzozero described (in 1870) quite another fibrillar system in epithelium from the mouth, vagina, and in the intermediate region between skin and mucous membrane, —that the cells possess a fine, short, prickle-coat, formed of fibrillæ, which lay on the surface and produce saw-shaped elevations. He claimed the discovery of interspinous spaces which has been attributed to Ranvier, and we must admit that he, moreover, perceived the continuity relations of the cells by connecting links.

Heitzmann, in 1873, tried to prove in his new theory of protoplasm and cells that all epithelium was continuous through spoke-like living threads; and, although his view of the obliteration of all chemical and histological distinctions in the cell constituents—the cell substance, nucleus and nucleoli—is by no one now accepted, his scheme was at first taken up by many. The author states his reasons for

... ...minality of epithelial cells
... ...accepting their continuous con-
... ...appears to him, from
... ...the sheaths of the prickles
... ...rational to assume that
... ...which at first exist in small
... ...remains never become dis-
... ...and pathologically, this con-
... ...quick-growing epithelial
... ...normal epithelium, the free
... ...growing cell at one side,
... ...and in a simple
... ...may be so expanded and
... ...may be shrunken or
... ...with the neighbouring
... ...necessary character, the
... ...the epithelial cell; but,
... ...vitle phenomena dis-
... ...connected together
... ...cells must therefore
... ...the epithelium is in-
... ...the transmission of
... ...frequently changing,
... ...the cell. Although
... ...of Bizzozero, he
... ...a portion, like this
... ...Harvey, nor rolling
... ...because all these ex-
... ...does not exist.
... ...al effect may give
... ...of a fibre, and this
... ...Between the
... ...and when these lie
... ...processes, but not in
... ...produced. The long
... ...screening, because
... ...processes.
... ...view (1887) that the
... ...protoplasm" of the cells,
b... ...through the stroma

of the protoplasm, and merges in neighbouring threads of hyaloplasm. That observer gives no detailed proofs of this supposition, which is against all experience hitherto. The upshot of all researches up to the present is that the cutaneous epithelial cell-body is filled with fibrillæ, which encircle the nucleus, and by means of connecting processes extend from one cell to another (Ranvier). The function of the latter is so far unknown. Each connecting bridge consists of such a thread, enveloped by a continuation of the cell-mantle, which later becomes cornified (Cajal). The epithelial cells show their full individuality, especially in pathological formations, and their prickles merge again, if parted, without any visible swelling—which does not, as a matter of fact, exist in the connecting processes.

## The Nail.[1]

Our knowledge of the histology of the nails has been enriched by some observations of Henle.

Ranvier, before the appearance of Henle's work, has denied the existence of "Eleidin," either in the nail itself, in its matrix, or in the bed of the nail, and so far he agreed with Unna's views and Heynold's. He found, however, that a peculiar substance, which he called the "onychogenous material" or "onychin," occurred in the transitional cells of the matrix. This "onychin" was easily identified by its being stained brown, and not red, by picrocarmine. Suchard described this substance as occurring, not only in the matrix, but also in a thin layer in the bed of the nail.

The brown colour of the zone of transitional nail-cells, first described by Unna in 1875, is recognised by all observers, but is differently explained by them. Whilst Waldeyer finds keratohyaline, Ranvier, Suchard, and Henle recognise a new granular material, "onychin," in this area, Eulsberg and Unna find neither of the two present. Differences of opinion exist therefore only as regards the nature of these brown granules; all observers are of one opinion as to their existence and their position.

[1] "Die Fortschritte der Haut Anatomie in den letzten 5 Jahren," 'Monatsh. f. prakt. Derm.,' Bd. viii, 1889, No. 2. IV. Der Nagel.

Henle states that the "onychin" extends only as far as the white edge of the lunula, and that its boundaries are here sharply defined; he disagrees with Suchard as to its being prolonged in a thin layer over the bed of the nail. He goes on to state that 2—4 rows of cells contain this onychin, and that the breadth of this transitional zone increases from the posterior edge of the groove forwards.

The author quite agrees with these observations if, instead of "onychin-holding" cells, we read transitional cells. The existence of a special nail-forming substance seems to him to have been no more proved by Henle than by Ranvier and Suchard.

Henle is, in Unna's opinion, quite right in now considering that the epithelial swellings, ridges, and papilla at the base of the groove vary very much in different individuals, as Blaschkos has shown. From the anastomosis of the two digital arteries small vessels are given off which run forwards, lying parallel to each other, and, in the first part of their course, are very twisted. They do not give off any branches, and have only a few communications with each other and with the deeper vessels of the bed of the nail. More anteriorly these vessels are narrower, and lie in a deeper plane; the difference in vascularity of the posterior and anterior sections of the root of the nail depends on this fact, and not on a diminished blood-supply.

The richer blood-supply of the bed of the nail, as compared with the anterior part of the matrix, is thought by Henle to be due to the fact that, at the groove, the nail is nourished on two sides; on the bed, however, only on one side; it requires therefore a greater blood-supply in the latter situation.

From some observations of Egenbauer, Zander, and others, on the comparative anatomy of the nail, some details in their development in the fœtus become intelligible. Unna described in the human fœtus a furrow which lies in front of the bed of the nail, which produces, in the last months of fœtal development, a large mass of horn. He showed further that the growing nail spreads itself over this horny mass in a thin layer, and that this horny material, together with the thin edge of the nail, is mostly shed after birth. This horny

proliferation at the anterior part of the bed of the nail was up till now not understood, but it is now clear. It represents the horny pad of animals, and its active, but evanescent, production is the remnant of a former greater and more lasting development of this epidermic material.

The author then goes on to give an account of recent publications on the development of the nails by Zander, Brooke, von Köllicker, and Gegenbauer. We are indebted to Zander especially, he says, for the first detailed description of the eponychium in its different segments, and for the first exact account of the granular cells which appear below it during fœtal life, to disappear with it later.

These cells of the embryonic nail-bed must not be confounded with the granules of the "granular area," the root-sheath, or the medulla of the hairs; and at present we can not speak of a "granular layer" of the nails, but we must use the expression "granular cells of the embryonic nail."

In conclusion, the author states that our knowledge of the development of the nails has been materially increased by these observers, and that the most interesting questions of the future will be as regards the nature of the granules below the primitive nail (which one might call "onychin"), and also as regards the character of the most superficial strata of the nail itself.

## The Nerves of the Skin.[1]

Some observations of Pfitzner's on the nerve-endings in the tadpoles of frogs and newts led the author to investigate these endings in the human skin; and he described the cutaneous nerves as ending in the prickle-cell area in two intra-cellular nerve-bulbs or swellings. His and Pfitzner's views have not been generally accepted by histologists. W. Wolff denies the existence of the subepithelial network of nerves, which, according to Pfitzsner and Canini, gave

[1] "Die Fortschritte der Haut Anatomie in den letzten 5 Jahren," von P. G. Unna, 'Monatsh. f. prakt. Derm.,' Bd. viii, 1889, No. 5. V. Die Nerven der Haut.

off vertical branches to the epithelium. He states that the nerves end in sharp points below the epithelium.

Mitrophanow published a more exhaustive account of the same subject, and arrived at the following conclusions:— That the peculiar structures described by Eberth are not nerve-endings at all, and that the fibres, given off to them from the subepithelial plexus, are not nerve- but connective-tissue fibres; he denies the existence of this subepithelial plexus altogether. The nerves given off from the subcutaneous, so-called fundamental, plexus he finds do form bulbous endings in the epithelial layer, but these are between, and not in, the cells. From his observations on the frog he disagrees with Unna's views on the nerve-endings in the prickle-cells in man.

Frenkel disagrees with Mitrophanow's idea, and finds that the cutaneous nerves in the frog have intra-epithelial terminations. Frenkel has also published a paper on the nerve-endings in man, in which he first discusses the three chief varities of epithelial nerve-endings (viz. ending within special cells, within ordinary epithelial cells, and between the epithelial cells), and then gives the results he has arrived at by staining with chloride of gold and osmic acid.

By staining with gold, numerous black threads and networks of threads, which give off vertical branches to the epithelium, are seen; but he cannot find that these have any communications with larger nerves, and he thinks they are caused by deposits of gold.

By treating sections with osmic acid, he finds numerous threads and granules within the cells, which correspond to those described by the author, but he can find no connection between these intracellular threads and the intercellular ones. The threads are never seen to pierce the cells, and Frenkel looks upon them as threads of protoplasm which the cells in shrinking has pulled inwards with it.

He thinks epithelial nerves do exist. The delicacy of the nerves of each and the stiffness of the epithelial covering necessitate that the nerves should be in close relation with the epithelial cells; the nerve-endings must, in fact, be in the cell itself. He then raises the question as to

whether all the epithelial cells are supplied with nerves or only some of them. Frenkel thinks that only some of the epithelial cells have direct nervous functions, but that all of them have them indirectly, since, by lying in continuity with each other, they are capable of transmitting nervous impulses.

The most important question Unna thinks, and one upon which these observers do not throw much light, is whether the intra-cellular nerve-ending in the human prickle-cells, as described by him and Pfitzner, are of universal occurrence. Macallum has stated that, in the tadpole, Eberth's structures are the sheaths of those nerves which enter and terminate next the nucleus in the cells, whilst other nerve-terminations are found between the cells. This arrangement of nerve-terminations, partly inter- and partly intra-epithelial, is exactly the same as the author's description of the terminations in human skin.

We are indebted to the Hoggans ('Linnean Soc. Journ.,' 1882) for a close study of the nerve-endings in mammalia. They began their work by studying the habits of captive moles, and then went on to make detailed comparisons between the nerve apparatus of hairs and those peculiar collections of intra-epithelial nerve-terminations, which are known in the mole as "Eimersch's organs." Of importance to us is the survey of the nerve apparatus of hairs. They distinguish three kinds:

(1) Medullated nerve-fibres, which are distributed to the hairs.

(2) These, by breaking up, give rise to (*a*) branched ganglia among the lowermost cells of prickle-area of the sheath of the hair; (*b*) forked non-medullated parallel fibres, which, in numbers varying from one to four, run parallel to the axis of the hair; (*c*) a bundle of non-medullated fibres which surround the forked ends of the above, and are situated just below the mouths of the sebaceous glands.

(3) Intra-epithelial non-medullated varicose fibres, which are distributed in the prickle-cell area of the hair.

While 300 to 400 nerves are supplied to the large "touch-hairs" of the horse, one to two nerves supply each ordinary hair, joining it about the middle of the sheath, and dividing into

two or more branches, each being provided with a nerve-ending.

G. Hoggan, in another paper, collects in five groups the known methods of nerve-termination in the skin of mammalia.

(1) Non-medullated nerve-fibres of the subepithelial plexus which accompanies the blood-vessels.

(2) Meissner's touch-corpuscles. Groups of ganglia, connected to each other by non-medullated, to the centre by medullated, fibres, and which, according to Hoggan, only occur on the palmar and plantar surfaces of man, monkeys and marsupials.

(3) Forked endings, occurring in ordinary hairs, less often in "touch-hairs."

(4) Pacinian bodies.

(5) Segregated nerve-cells, separated by epithelial cells, in the basal prickle-cell area; these are Merkel's "touch-cells." Hoggan adds to these three others modes of nerve-termination.

Goldscheider examined small pieces of the skin of his forearm, and he has described the distribution of nerves to the various sensitive "points." He finds that mixed nerve-bundles run up to the surface of the sensitive areas, and that the nerves which suppy the "temperature points" run with the vessels, while those supplying the "pressure-points" lying parallel to each other are distributed.

Goldscheider thinks that the difference between "cold" and "hot-sensation" areas lies in a molecular distinction between the two sorts of nerve-endings.

He points out the importance of the absence of touch-bodies in the "touch-points." These bodies, from their limited distribution, were always considered not to be essential for the sensation of pressure. Goldscheider, in conclusion, points out that the "temperature nerves" do not feel the prick of a needle, and he considered them, therefore, to be analgesic.

## The Pigment of the Skin.[1]

Unna stated, in 1876, that the matrix cells of the cortex of the hair were contained in envelopes of pigment; he acknowledged, however, that higher up in the shaft, and in cases of marked pigmentation, the pigment might find its way into the cells themselves.

Waldeyer entirely opposed these views, and stated that the pigment was contained in the formative cortical cells at the lower end of the hair.

Riehl, in 1884, showed that the pigment was situated in irregular-shaped migratory cells below and in the papilla, and was carried up in these into the interstices between the epithelial cells. Higher up it disappeared from these interstitial spaces and accumulates in the protoplasm of the epithelial cells.

Aeby, at the same time, stated definitely that pigment is not formed in the epithelial cells, but is carried thither and deposited there by migratory cells from the connective tissue.

Ehrmann conducted some experiments on frogs and guinea-pigs, and found that, when ecchymoses had been caused in these animals, the colouring matter of the blood taken up by the cells was transformed into amorphous granular pigment, whilst hæmatoidin crystals were also formed in the tissues. These same tissues were later found to contain large quantities of pigment in the cells of the cutis and the prickle-cell area of the epidermis. He deduced from these experiments that pigment originates from the colouring matter of the blood, which the connective-tissue cells closest to the vessels take up; these cells, he states, do not migrate out of the cutis, as Riehl and Aeby supposed, but merely pass the pigment on to the cells of the epidermis. In man, Ehrmann states, pigment is entirely formed in the cutis, although it is almost only found in the epithelium; he forms this conclusion from the analogy of the skin of am-

[1] "Die Fortschritte der Haut Anatomie in den letzten 5 Jahren," 'Monatsh. f. prakt. Derm.,' Bd. viii, 1889, No. 8. VI. Das Pigment der Haut.

phibia, in which the origin of pigment in the cutis is more easily observed, and also from the fact that in cases of deep pigmentation pigment-cells are also found in the cutis. The author agrees with Ehrmann that leucopathia syphilitica, vitiligo, and poliosis depend, not upon recession of pigment from above, but upon a cessation of supplies of newly-formed pigment from below. He considers the chief value of Ehrmann's work to lie in his experimental and histological proofs of pigment-formation in the cutis, and also in his descriptions of the transference of pigment, without any change of position in the cells of the cutis which contain the pigment. He considers Ehrmann's theory of separate cells in the epidermis passing the pigment upwards to be far-fetched and untenable.

Karg showed that a portion of white skin, grafted on an ulcer in a negro, became very soon quite black, and a portion of a negro's skin, grafted on to a white man, very soon lost its colour He agrees with Riehl and Aeby that the transference of pigment is carried out by "wandering" cells —chromatophores. After reviewing some publications of Nothnagel and von Köllicker, Unna sums up by saying that upon one point at least all observers are agreed. Pigment does not originate in the epidermis, but is transported thither from the cutis. Further, that in the lower epide rmic strata the pigment lies between the cells, and makes its way higher up into the cells themselves, where it collects especially at the distal pole of the nucleus. Disagreement exists as to the means by which the pigment is carried upwards. Curiously enough the lymph-stream has not been mentioned by any observers as a probable means of conveyance of the pigment, and to Unna this seems the most plausible theory. He thinks that the pigment reaches the anterior of the cells along the channels by which the intra-cellular nerve-filaments, described by him, are distributed.

ON

# THE NORMAL SURFACE AND COVERING OF THE TONGUE.[1]

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In this paper the author does not propose to deal with the posterior part of the tongue, with its circumvallate papillæ, as this region is often hardly in view. We must distinguish between the dorsum and the edges of the tongue; and in every description of these two regions, always lay particular stress upon the colour of the organ and the condition of its surface. The colour is determined by the circulation and the condition of the epidermic layer, the smoothness of the organ by the mode of distribution of the papillæ, a constantly varying factor, and also by the condition of the epidermic layer.

(1) *The circulation.*—Anæmia and venous congestion cause a bluish-grey colour of the tongue, while a good circulation is indicated by a more or less red, fleshy colour. When some persons put out their tongues anæmic patches are seen, especially along the median line, which are caused by contractions of a few bands of the transverse muscle.

(2) The condition of the epidermic layer demands a far closer inspection. We know that this surface varies very much in the distribution of the filiform and fungiform papillæ. When the filiform papillæ are long and cover the

[1] "Ueber die normale Zungenoberfläche und der normalen Zungenbelag." 'Separat-Abdruck aus der Vierteljahresschrift für Derm. and Syph.,' 1881.

whole surface, the tongue looks whitish in colour and very rough ; when, on the other hand, the length of the papillæ, with the hair-like processes, is gradually lessened from behind forwards the tongue is redder and smoother towards its edges. The length and thickness of the tufts of hair-like processes of the papillæ influence the appearance of the surface of the organ. The longer these processes are the whiter does the tongue appear, and, when they have reached a certain length, what we may call a normal furred tongue is the result, which the practical physician is always rather prone to look upon as pathological.

The presence of a fur upon the tongue depends, therefore, normally as well as pathologically, upon the length of the processes borne by the filiform papillæ; and, unless we know the usual condition of a tongue beforehand, it is hard to say whether a fur is pathological or normal. A pathological fur is formed upon the tongue by a swelling of the hair-like processes of the papillæ, which become thicker and longer, and together appear as a thick, white, homogeneous fur. The increase in thickness of the whole epidermic layer depends upon a swelling of the individual cells, and the pronounced whiteness upon the same cause, well as upon a loosening of these cells which leads later to the removal of the fur. This is the simplest and commonest form of fur as met with in gastric derangements.

As regards the fungiform papillæ, these contain more connective tissue, but a smaller horny covering, than the filiform papillæ. The epidermic layer forms a horizontal covering over them, and is not, as in the case of the latter, prolonged up into delicate processes. Sometimes the fungiform papillæ approach in construction to the filiform, and stick out on the surface of the tongue above them. More commonly, however, the filiform are shorter and thicker than usual, and then the tongue has a markedly smooth appearance; this is often seen in old and wasted individuals, and depends in this case upon atrophy of the papillæ.

The red colour of the fungiform is in marked contrast to the whitish colour of the filiform papillæ.

One can easily imagine the different types of tongue which result from the various modes of distribution of these

papillæ. As the fungiform papillæ affect the edges of the tongue, these usually appear red.

A common arrangement is for the fungiform papillæ to form clusters, as large as a pea or cherry, along the edges or dorsum of the tongue; sometimes they form three or four parallel rows along the edges, and are entirely absent from the dorsum. They are sometimes all collected together at the tip of the tongue, which then appears red and granular.

There must be mentioned, in conclusion, the linear absence of papillæ which causes furrows along the surface of the tongue; a median longitudinal groove is the commonest. Rarer are vertical grooves, at a distance of about ·5 cm. from each other, which cause a most peculiar appearance of the edges of the tongue. Another curious appearance arises when the whole surface of the organ is covered with furrows, then looking something like convolutions of the brain.

# ON THE INSENSIBLE PERSPIRATION OF THE SKIN.[1]

It is certain that in the every-day treatment of skin diseases we exert, by means of ointments, powders, plasters, varnishes, &c., a considerable influence upon the physiological functions of the skin as regards the evaporation of water and the secretion of fat. To study the conditions of this evaporation the author closed a funnel with the skin of a fowl (cutis and epidermis) from which the fat had been removed, and connected it with a graduated glass tube which indicated the amount of water lost by evaporation through the skin. By this means he was enabled to judge of the difference in the amount of evaporation caused by the application of varnishes, &c., to the skin. Four of these funnels were placed side by side in a box, and the amount of water lost by each could be read off on the graduated tubes with which these were connected. The amount of water lost by evaporation was, as one would suppose, lessened by fats, and lanolin prevented evaporation more than any other. This obvervation was interesting, as it is well known that the skin becomes slightly swollen and more turgid after the application of lanolin ointments than after ordinary ones of the same strength, and we know that our drugs act more powerfully upon the skin, in proportion as the epidermis becomes more turgid, by the retention of the water of evaporation. Glycerine also prevented evaporation.

In exact opposition to the fats is the action of "gums."

[1] "Ueber die insensible Perspiration der Haut." IX. Cong. f. inner Med.

It is a well-known fact that by the application of gum to the body large quantities of bodily heat are withdrawn. A man covered all over with gum shivers in a well-warmed room or in bed. This fact is explained in various publications, in which the author recommended gum in certain skin diseases, as due to an increased evaporation by the skin. This evaporation through a porous body, as dried gum is, seemed to be natural enough. The experiments with the above apparatus have, however, definitely proved that, with a thin coating of gelatine, the amount of water lost by evaporation is increased, and that the gelatine had therefore an exactly opposite effect to ointments. Experiments were then made with equal quantities of collodion, gutta-percha, and india-rubber. The covering of gutta-percha diminished the amount of evaportion to a third, the one of indiarubber down to one seventh, while the covering of collodion did not only not diminish the amount, but actually increased it by two thirds of its former amount. A thin covering of collodion allows therefore about ten times as much water to evaporate from the skin as does a covering of india-rubber. Further, we can state that, so long as a thin covering of collodion or gelatine sticks close to the skin, it not only does not prevent evapora tion, but actually increases it.

It is a matter of every-day experience that starch-powder has a beneficial effect on cutaneous inflammations, not only on moist, secreting surfaces, but also on merely hyperæmic ones. Dusting the inflamed surface with powder has a cooling effect, and exerts this by increasing the insensible evaporation from the skin. This is brought about in the following way:—The powder removes by capillary attraction the particles of fat from the skin, distributes these over its whole surface, and thereby allows of freer evaporation through the epidermis. It is for this reason that the application of powders has its most cooling effect on the skin of the face, where the inflamed areas are most fatty.

By modern physiologists the important evaporation of water by the skin is looked upon as a sort of perspiration, and no clear distinction is drawn between skin-vapour and sweat. When we consider that the amount of water lost by evaporation reaches in the twenty-four hours 1 kilo. (Séguin) or

½ kilo. (Weyrich), we can hardly understand how recent works on physiology have laid so little stress upon it.

Some practical results must, in conclusion, be pointed out which may be deduced from these experiments. If we cover the skin of a healthy individual with fat, *e. g.* a mixture of lanolin and vaselin, he will lose very much less water through his skin. Less heat is given off, and more water is passed through the kidneys. The storing up of heat is probably the object aimed at in rubbing atrophic and wasted children with fat and oil. If, on the other hand, we have a poison circulating in the blood, which we know will certainly not be got rid of through the skin, but through the kidneys, it would seem to be rational treatment to cover such an individual with fat, so as to drive more water through his kidneys. On the other hand, we are possessed of remedies, as we have seen, which materially increase the insensible perspiration. We can effect this by the removal of fat from the skin, and, in a greater degree, by smearing the body with gum. This latter method has been in use in skin diseases for years. If, therefore, we wish to increase the amount of perspiration, we cover the body with gum; and, to carry out this treatment effectually, the covering of gum must be washed off and renewed every third or fourth day. This seems to be a rational mode of treatment in pyrexia, where unloading of the kidneys is called for, and this method the author recommends to the consideration of physicians.

# ON SKIN VARNISHES.[1]

In the therapeutics of skin diseases film-forming applications, or, as the author prefers to call them, "varnishes," play a peculiar part.

Theoretically one might not expect much benefit from their use; but experience teaches us that these applications do good, and efforts are always being made either to enlarge their number or to improve existing ones.

It is certain that very satisfactory and far-reaching results are obtained by the use of varnishes, which have apparently only superficial effects; but we do not know how to specify suitable cases, nor can we give a scientific explanation of the therapeutic effects of these applications.

At the International Congress in Washington in 1887, Dr. Knaggs, of London, read a paper "On a New Method of Local Treatment in Skin Diseases," and in the ensuing discussion the author gave his classification of varnishes, as follows:—

(1) Æthereal or benzin solutions or india rubber, nitrocellulose, gutta percha, aluminate; (2) Spirit solutions of resins, wax, fats, oleates, and soaps; (3) Watery emulsions of the last-named; and (4) Watery solutions of gum, dextrine, albumen, gelatine.

The author, at the Congress in Vienna in 1890, gave some details on the different permeability of various varnishes by aqueous vapour, which were more or less diametically opposed to the popular views on this point.

[1] "Zur Kenntniss der Hautfirnesse. Versamml. Deutscher naturf. in Aerzte in Halle, 'Therapeutische Monatshefte,' Berlin, November, 1891.

Elliot, of New York, has lately advocated the use of "Bassorin" as a basis for varnishes. "Bassorin" or traganthin" is found in some varieties of gum plants, and is distinguished from gum by its behaviour when treated with water. It does not dissolve as gum does, but swells up especially in hot water, into a tough slimy mass.

The author had used tragacanth, which consists chiefly of arabin and bassorin, in the form of varnishes and ointments for a number of years. Elliot, however, introduced a material, made from this traganthin, which excels the gelatin preparations in homogeneousness; but he does not tell us how his dispenser prepared this substance; we are merely informed that "bassorin-paste" consists of "bassorin, mixed with glycerine and dextrine. The author examined some samples of this preparation, which Elliot sent him, and found that the basis of it consisted not of tragacanth itself, but of the purer, slimy substance—bassorin. Beiersdorf has obtained a very nice, homogeneous preparation by rubbing tragacanth up with water and then filtering; the filtrate being then condensed by evaporation and mixed with glycerine. In this way a preparation, having the same properties as Elliot's paste, has been obtained, without the addition of dextrine being necessary.

Beiersdorf also made a bassorin varnish, which contained a good deal of starch, by treating lumps of "Salep" with water, condensing the slimy mass by evaporation and adding glycerine.

These two bassorin varnishes have the advantages over the Traganthin varnishes, formerly employed by the author, and lately recommended by Pick—in containing more bassorin—(5 to 2½ per cent.), and in the film their form being, in consequence, smoother and firmer, and, at the same time, more delicate. They also spread themselves much more evenly over the skin.

Both these varnishes are readily miscible with oxide of zinc; while most of the varnishes in use are not.

The author then goes on to make some observations on other skin varnishes, which are soluble in water, and of these the casein preparations are the best.

Casein powder is dissolved in an alkaline solution, the

best alkali for this purpose being borax. It has been found that the following proportions gave the best film on drying :— Casein, 5 ; borax, 0·6 ; water, 25, or 20 per cent. casein + 2½ per cent. borax. This solution dries quickly and forms an even, smooth film, which readily takes up various drugs, such as resorcin, pyrogallol and even chrysarobin, without any oxidation taking place.

If casein is dissolved in ammonia, which is allowed to evaporate, then mixed with glycerine, a fine emulsion results ; and the casein keeps its film-forming proporties. This glycerine-casein-varnish is very elastic, dries easily, forms excellent films, and is compatible with most drugs.

The author gives the five best balsamic and resinous varnishes.

(1) *Amber varnish.*—The amber-lac of commerce is a mixture of amber and turpentine, dissolved in alcohol. It is an excellent vehicle for chrysarobin and pyrogallol, drying quickly, and forming a pliant, smooth film, which can be easily removed by cotton wool dipped in spirit.

(2) *Castor-oil shellac varnish.*—Solutions of shellac in alcohol are useless, for they are too brittle. A good varnish is obtained by mixing shellac one part, with castor-oil one fifth part, and alcohol three parts ; and this when filtered, is miscible with zinc oxide.

(3) *Canada-balsam-collodion varnish.*—A mixture of 16 parts collodion with 1 of Canada balsam forms a clear, pliant film, which takes up oxide of zinc better than No. 2, and is also miscible with pyrogallol, though not so well with chrysarobin.

(4) *Castor-oil-collodion varnish.*—Eight parts collodion and 1 part castor-oil, with 1 part zinc oxide, make an excellent varish with oxide of zinc, which undergoes no decomposition.

(5) *Lead-ricinoleate varnish.*—One part of oxide of lead is boiled with 1½ parts of castor-oil ; and this dissolved in 2 parts of absolute alcohol forms a good varnish. A large quantity of oxide can be incorporated with it.

The author gives the following formulæ

(1) ℞ Acid. Salicylic., 3.
Canada balsam, 1.
Collodion, 16.

(2) ℞ Zinci. Oxyd., 2.
Ol. Ricini, 2.
Collodion, 16.

(3) ℞ Resin, 5.
Ol. Ricini, 1.
Pyrogallol, 1.
Alcohol absol., 15.

# THE ACTION OF CARBOLIC ACID AND OIL OF CLOVES ON LUPUS.[1]

Besides tuberculin, two drugs, carbolic acid and oil of cloves, have a specific action on lupus tissues when applied locally. A concentrated solution of carbolic acid causes a dry scab, which is scarcely raised above the level of the surrounding skin, and the necrotic tissue is removed without any moisture.

The application of oil of cloves acts differently. Only a superficial scab is produced, under which the cutis becomes raised and swollen. By continued application of both drugs, the epithelial covering of the lupus nodules is destroyed, while that of the healthy surrounding skin remains intact.

Occasionally, more often with oil of cloves than with phenol, the epidermis is raised up in blisters, and then ulcers are formed.

The author has examined sections of lupus nodules, with the healthy surrounding tissue, twenty-four hours, two days, and seven days after treatment with carbolic acid.

The most noticeable feature in all the preparations is the scabbing of the epidermis, and later on of the cutis. In specimens in which the treatment has lasted one or two days, an upper necrotic layer of epidermis, and a lower apparently healthy layer, separated by a deep line of demarcation, cover the lupus nodule.

If the action of the carbolic acid be continued, the whole

[1] "Die Einwirkung von Karbolsäure und Nelkenöl auf Lupus Gewebe," 'Monatsh. f. prakt. Derm.,' xiii Bd., 1891, p. 463.

epidermis becomes necrotic, and the distinction between the cells and their nuclei disappears.

The action of carbolic acid is always more pronounced on the epithelium of the lupus nodules than on that of the surrounding healthy tissues.

A " reaction of the epidermis " takes place, which for some time prevents the further destruction by carbolic acid. These changes are worthy of consideration.

The configuration of the epithelium undergoes great changes, the sub-papillary prickle-cell area alone retaining its form ; the supra-papillary, on the other hand, is attenuated and, in many places, is only represented by a few rows of cells. A horny layer, consisting of only a few rows of cells with horizontal rod-shaped nuclei, is spread over this prickle-cell layer, and forms the line of demarcation of the necrotic change.

When the " reaction " takes place, changes are observed in the prickle-cell area. It becomes thickened and the supra-papillary portion is seen to be composed of two layers. The upper one of these is thickened by œdematous swelling of the older prickle-cells, and is composed of large clear cells with slightly stained nuclei, while the lower layer is composed of small deeply stained cells rich in chromatin.

It is this altered prickle-cell area which, in conjunction with the thickened epidermis, prevents for a long time the action of carbolic acid on the under-lying tissues.

Carbolic acid acts upon the cutis very much in the same way, and acts much more deeply upon lupus growths than upon healthy surrounding skin. The collagenous tissues in the connective-tissue layer lose their fibrous structure and become homogeneous ; they blend with the protoplasm of the connective-tissue cells, to form a structureless mass in which the nuclei of the cells are seen lying. The further action of carbolic acid upon the skin causes greater disorganisation. The structureless homogeneous mass becomes split up in every direction and assumes a porous, worm-eaten appearance.

As carbolic acid has a preference for attacking, and causing molecular destruction of, the older and already disorganised tissues, we can easily understand its action on lupus. According to the author's experience, applications of strong carbolic

acid have occasionally, without other treatment, caused the disappearance of lupus nodules. The number of applications must be regulated by the depth of the nodules, they must be carried out continuously without allowing the skin to recover. Pure carbolic acid must be used.

We may now consider the effect of oil of cloves upon lupus and the surrounding healthy skin.

After two days' treatment, we find the epidermic and granular layers of the healthy surrounding skin somewhat thickened, while those covering the lupus nodule are transformed into a scale. The prickle-cell area remains passive under this treatment; and even after seven days' application, we only notice a slight enlargement of the cells and an increase in the nucleolar bodies, 2 to 3 in each nucleus.

It is only after long-continued use of the oil that degeneration of the epithelium takes place. The necrosed portion of epithelium is not so sharply defined from the simply œdematous portion, as after the application of carbolic acid, although we can, in this instance too, speak of a line of demarcation which is marked out by a row of minute vesicles.

The epithelium covering a lupus nodule, after treatment for weeks with the oil, is sometimes found to be softened and permeated with serum and fibrin, but with only a few leucocytes; or it may have fallen off as a scale. The action of the oil on the cutis elements is not so sharply defined as that of carbolic acid. The action extends deeper in a few days than that of the acid, but the resulting changes in the lupus nodules are very much the same. These changes, however, occur more rapidly; even after two days, the lupus nodule is broken up by numerous cracks, and has a finely porous appearance; and after some weeks it appears spongy, and is riddled with holes.

In conclusion, the author considers that the therapeutical value of oil of cloves can not be compared with that of carbolic acid.

ON THE

# CULTIVATION OF EPIDERMIC FUNGI.[1]

In Dr. Unna's first communication on that form of eczema to which he gave the name "Eczema seborrhoicum" (on account of its connection with the so-called "Seborrhœa sicca," and of the fatty nature of the exudation), he stated that he had no doubt as to its parasitic origin; and he has since then been investigating the fungi occurring in the pathological products of the affection. These researches were continued with the help of Dr. P. Taenzer, and the conviction became paramount that, in order to determine a particular fungus as the only final cause of the disease, it was absolutely necessary to study all recently discovered botanical facts in reference to the skin fungi in general. By means of Koch's method of plate cultures with the scales and secretions of Eczema seborrhoicum, an astonishingly rich flora became apparent, and every new case of the disease added new parasites to those already found; so that it was impossible to arrive at even a preliminary conclusion by this means.

Twelve typical cases were thus mycologically studied, in order to become acquainted with the botanical aspect of the question, without reference to the ætiology of the disease. This inquiry gave, from about 60 pure cultures, 50 different mucors, over 20 varieties of Penicillium, 5 Aspergilli, about

[1] "Die Züchtung der Oberhautpilze," 'Monatshefte für praktische Dermatologie,' vii, 1888, No. 10.

a dozen belonging to the Oidium and Saccharomyces group, 3 common yeast fungi, and a considerable number of cocci and bacilli—some known and others unknown. All these were obtained with weak alkaline media—viz. the ordinary peptone-gelatine and agar—and at the temperature of the room. There is no doubt indeed that other conditions, acid media, growth upon potato, apple, vegetable decoctions, &c., and higher temperatures, would have brought into development, and therefore to our knowledge, a fresh multitude of plant germs. Similar conditions were employed in these experiments because we know botanically that certain fungi have been formerly taken to be of distinct kinds, while only differing in consequence of varying surroundings. Fungi, macroscopically and microscopically distinct, systematically cultivated alongside of one another for a considerable period (six to eighteen months) on the same media, and at the same temperature, and always presenting the same characteristic, must represent distinct kinds. Not until these have been definitely identified, is it worth while mycologically analysing further cases of the same skin disease with other media and higher temperatures, &c. But what purpose, it may be asked, does the investigation of this legion of fungi serve, where it is *a priori* certain that only a twentieth or perhaps fiftieth part of them produce a really pathological action, the rest being harmless accidental parasites? Is it not enough to test all pure cultures by inoculation, and to direct attention only to those which show positive results? In point of fact, the first pure cultures were inoculated in the skin of three healthy medical men; and these experiments showed that it would be an error to rely on the simple requirements of modern bacteriology, without modification, when dealing with the ætiological meaning of a schizomycete in reference to an epidermic disease. Most parasitic epidermic affections (Parakeratoses) injure the general health but little; and then only through acompanying nerve irritation. The fungi find an insurmountable wall in the normal vascular connective tissue, and they cannot—as the laity and alas! many physicians still believe—"Strike in," overflow into the circulation, and thereby endanger the general health. Those skin fungi which can do this—like the streptococci of erysipelas, the pus-forming

staphylococci, the bacilli of lupus, lepra, syphilis, the parasites of smallpox, scarlatina, measles, rötheln, &c.—are at present out of consideration. The ordinary method of investigation being here inapplicable, viz. the injection of pure cultures into the blood, subcutaneous tissue, anterior chamber of the eye, and peritoneum, we are led to inoculate the epidermis directly. Negative results, however, with this method can have but little value. There is no certainty of being able to induce the epidermic fungi to grow in the skin, and we do not even know the principles of the methods which should be used. An incision into the vascular connective tissue, as in the case of inoculation with vaccine, cannot be requisite, but, on the contrary, may even hinder the growth. Is it possible that a stronger hyperæmia is necessary for the fixation of the spores? Should the skin be kept dry or damp, covered or uncovered, in the light or in the dark? What parts of the surface, and what reactions and other conditions of the skin are requisite? On the whole, we can now only give the unsatisfactory answer to these questions that these conditions vary with the fungi, and according to the kind and locality of the dermatoses generated. We may inoculate fungi which are found in Eczema seborrhoicum in the flexures, which have many coiled glands; the fungus of Pityriasis versicolor in dark places, and so on; and we shall find as a result at least that many fungi vegetate on some parts of the epidermis luxuriantly, and not at all on others. Individuality certainly plays nowhere a greater rôle than with the parasitic keratoses. If this were not so, they would be contagious, in the common sense of the word.

In these inoculation experiments pure cultures containing the spores were gently rubbed in over the skin (previously cleansed with soap and water, and alcohol—not sublimate), which was not irritated or scratched. The left upper arm was generally used, and the spot covered with sterilized gutta-percha tissue glued down. The supposition was that any fungus which could grow at all in the horny layer, would also be able to make its way in without the latter being broken. The impermeable covering produced sufficient dampness and swelling of the horny layer, and sometimes even an erythema or a circumscribed *miliaria*

*rubra*. After three or four days the glued bandage was removed, and the place left to itself.

Negative results from this, or from any other method of inoculation, are not conclusive. The rarer a parasitic dermatosis may be, the greater must be the effect of individuality —physical and chemical constitution of the epidermis, and so much the less value must we assign to negative inoculation experiments. The relative slight inoculation power of the Trichophyton and Achorion must not lead us to assume the same for all the higher Dermatophytes. The instance of the Trichophyton teaches us what fine differences the medium produces. In one family, where all the members are subjects of this fungus, we regularly find that the younger children carry it on the scalp ; the elder ones on other parts, and but seldom on the scalp ; the adults never on the scalp—the men on the beard, and perhaps on other parts of the body. Inoculation with Trichophyton on an adult's head would almost certainly fail.

The above considerations as to the relatively small power of proof of negative results, together with the constantly increasing number of Dermatophytes, determined the author to neglect for the present the distinction of pathogenic and non-pathogenic species, but to study minutely each fungus for its own sake.

The various kinds were all found in the skin scales and secretions, and were able, under certain conditions, to vegetate in the nutrient soil, or at least to retain life. Apart from the botanical and general biological interest of this common source, this knowledge is important for every dermatological inquirer. The plan was therefore adopted, as a preliminary research, to work out a "Flora dermatologica," or rather, with the material of Eczema seborrhoicum, to commence the working out of such a Flora.

This Flora includes all mould- and fission-fungi which can be cultivated from healthy or diseased skin, and the products thereof—whether they are ætiologically connected with certain dermatoses, or originate without any real appearance of disease, or able to vegetate in the skin, or can temporarily maintain themselves there in a living state.

To attempt a systematic arrangement of these lower fungi

is just as unnecessary as impossible. On the one hand, we have at present no system for the lower fungi which could satisfy the botanists. For several—Penicillium, Oidium, Saccharomyces, allied to Trichophyton and Achorion, which we have good reason to consider true skin parasites—are now regarded in a totally different light to what they were a few years ago, and are even to some extent looked upon as lower growth forms of higher fungi. On the other hand, we medical men, with the information we have from Koch's methods of pure cultures, cannot blindly accept the system of postponement introduced in Botany in the last decade. From our standpoint, a doubt as to the certainty of the transformation by cultivation is quite justified.

The correct course, therefore, appears to be to give an unprejudiced account, macroscopically and microscopically, of each separate fungus, as chance brings it to light in plate cultures. The naked-eye characters are most important; for fungi in a large group, can be easily distinguished, whilst under the microscope they may separately appear very similar, and at first sight difficult to differentiate according to their mycelium or spore formation. The macroscopical differences are, therefore, to be preferred by the dermatologist as a temporary practical key to identification, after a cursory microscopical examination of the fructification has shown to which group—Mucor, Penicillium, &c.—the fungus may belong. The important differences in the macroscopic appearances are as follows:

1. *The colour of the fungus.*—This may be in reference to the upper surface of the fungus plot, or to the lower surface, or to the deeper layer of old cultures, a white stratum of aerial mycelium partly obscuring the tint; or the colour may appear in several layers. Moreover, it may occupy in some clusters only the centre, leaving the periphery white; in others, the outlying prolongations are likewise coloured; and some, again, show rings of different colours. With the age of the culture the tint generally changes; and many fungi communicate to the medium a special colour.

2. *The extension of the plot.*—Two characteristic types can be distinguished, showing an "unlimited" and a "limited" growth. Some fungi grow from the inoculation

streak, on both sides, or in a circular manner, over the whole surface as far as the nutrient material will allow. Others, after assuming from the point of inoculation a generally circular shape, do not grow further; and the small circumscribed plaques enter into their changes of age independently, and do not fuse together. This difference is possibly not without importance, for many suspected parasitic dermatoses can also be distinguished by their limited or unlimited method of growth.

3. *Growth in the inoculation puncture and into the nutrient medium.*—The diminishing amount of air in the inoculative puncture and in the deeper layers of the nutrient material will, obviously, cause just as many differences of growth with the mould fungi as with the Schizomycetes; and these can be used as macroscopic differentiating characters. Fructification probably never takes place inside the nutrient medium, but a hypha-formation may grow in as a downy mass, or thick bush, or a hollow cup, and show, besides the intensity of the growth, characteristics of great service.

4. *Peptonisation of the gelatine.*—Like the bacteria, the mould-fungi form two large groups, according to their liquefying the gelatine or not. Some impart to the liquid gelatine a characteristic colour; and the plot of fungus may float as a compact mass in the liquid, or portions may sink to the bottom.

For the final systematic classification of the fungi, microscopic observation is naturally of more importance. Medium powers, *e. g.* Hartnack's objective (Nos. 4 and 5), permit the examination of plate cultures without the assistance of a covering glass. We can easily distinguish in this way the form of the first body, the kind of hyphæ branches, and the fruit-bearers. Unfortunately, these are necessarily broken in order to examine them accurately with high powers; and many characters consequently are lost to us, especially the observation of *living* fungi.

The difficulty just alluded to, Dr. Unna has endeavoured to overcome by using a slide with a circular hole in the centre, in the following way: The slide is sterilised and temporarily closed on one side by means of a sterilised cover-glass, cemented on with vaseline. The slide with the cover-

glass beneath it is placed on a glass plate kept cool with ice, and the hollow thus formed in it is filled up with a mixture of peptone, gelatine, and peptone agar. As soon as the film of nutrient medium is solidified and adherent all round, the cover-glass is taken off, and about half of the jelly is easily removed by means of a heated platinum wire, a half-moon being allowed to remain on that side of the hole which, later on, is towards the lower edge of the slide, which is to be kept in a perpendicular position. The fungus is to be inoculated on the free edge of this half-moon, and the aerial portions naturally grow up into the upper empty half of the hole, parallel to the surfaces of the slide; *i. e.* the fungus grows in the plane of the latter. A series, twenty or more, of such slides, can be arranged, radiating from the centre, in a glass vessel lined with blotting paper, the inner lower corners resting on the centre of the bottom of the vessel, and the outer lower corners fixed in slits in pieces of cork, which are placed all round. The corks and papers must be previously soaked in sublimate solution. It is advisable to let the growth of the fungus proceed for some time before commencing the examination. A sterilised cover-glass is applied on one side, and in order not to contaminate the lower surface, it is as well to fix laterally on the stage of the microscope slips of cardboard, upon which the perforated slide can rest. We can now observe, with the highest powers, the fruit-bearers projecting free in the air, and uninterruptedly giving off spores or forming fruit-bodies; we can accurately see the form and budding of the hyphæ, partly in the air and partly in the nutrient substance; and, finally, we can use the hyphæ and fruit-bearers which have been accidentally pressed between the cover-glass and the nutrient disc for detailed observations and measurements.

While the ordinary plate cultivations are usually suitable for the flat growing fungi, these hole cultivations are especially useful for the upright growing forms, such as mucor. For those of medium growth a hole of sufficient size can be made with a platinum needle in the middle of the nutrient disc. This method is communicated in detail, as, according to the assurances of botanical authorities, no simple way of observing the growth of mould fungi has hitherto been

brought forward. It is hoped that it will prove useful to other workers.

With reference to the staining of the mould fungi, the author states that he does not at present possess sufficient experience to discuss the methods generally; there is no question that here, also, a rich harvest can be reaped by the earnest inquirer.

Dr. Unna promises to commence shortly, in conjunction with Dr. Taenzer, the publication of a "Flora Dermatologica."

# THE STAINING OF MICRO-ORGANISMS IN THE HORNY TISSUES.[1]

In order to study the harmful micro-organisms of the epidermis, we must have some reliable methods of isolating them by staining. This proof of the existence of the epidermic fungi has been neglected, and most bacteriological text-books are silent on the subject.

Von Sehlen was the first who succeeded in clearly differentiating between bacteria and epidermic cells by staining, and he was followed by Bizzozero, who published a method of double-staining and differentiation of the fungi from the cells.

These methods were, however, very tedious and somewhat clumsy. In 1885, Boeck by using a borax-methyl-blue stain demonstrated fungi in the skin, and he had, by the help of resorcin, finally improved our means of decolorising sections. At a meeting of the Medical Society of Christiania in 1887 he showed specimens of favus, microsporon, furfur, &c., stained with these dyes.

The author made a large number of experiments with various dyes, &c., and he states that we possess numerous methods which enable us to isolate by staining micro-organisms in the horny epidermis, nails, scales, crusts and comedones. These methods are not all equally useful, but are of different value for different micro-organisms.

To stain these micro-organisms, one proceeds as follows :

The epidermic scale (crust, comedo, &c.) is placed upon

[1] "Die Färbung der Mikro-organismen im Horngewebe," 'Monatsh. f. prakt. Derm.,' xiii Bd., 1891.

a glass slide and moistened with acetic acid. Another slide is placed crosswise over this one, and both are rubbed together until the epidermic scale is broken up into a sort of pulp. The two slides are then separated and rapidly dried over a spirit lamp, by which means the acetic acid is evaporated. The slides must be lifted, not drawn apart.

Each slide is then seized by the thumb and forefinger of the left hand, which is covered with a cloth, and is held obliquely upwards, while a few drops of ether-alcohol are poured over it. The fat, which had become liquified by the heat, is thus washed away, and absorbed by the cloth. Two drops of methyl-blue solution are then placed on one of the slides, which is then placed crosswise upon the other, and the two are held over the flame for ten to twenty seconds.

The specimens can then be either decolourised at once or dried over the flame, and kept for further observation.

In all cases, the author recommends borax-methyl-blue (1 per cent.) as the best staining medium.

Indirect decolorisation by alcohol and anilin oil, is much used in the preparation of sections containing epidermic bacteria; but the author prefers especially peroxide of hydrogen in combination with alcohol. Simple alcohol (80 to 96 per cent.) does not differentiate sufficiently; fungi and epidermis are decolourised too evenly.

The successive employment of peroxide of hydrogen and alcohol seems, however, especially useful for epidermic bacteria; for the epidermis is strongly acted upon by oxidising agents, and is always much more strongly decolourised than the micro-organisms.

Among a large number of reagents which dissolve anilin dyes, there are three which decolourise the epidermis quicker than the bacteria present in it, namely, styron, glycol, and glycerine-ether.

In the preparation of epidermic bacteria, indirect chemical decolourising agents are much used, especially acids. The chemistry of this method depends upon the fact that the basic anilin salts form soluble salts with the acids. The mineral acids proved to be of little use in this respect, but among the organic acids excellent decolourisers were found.

Formic acid and lactic acid gave good results; but citric and oxalic acids gave the best. Arsenious, osmic, sulphurous, and picric acids are also useful. Nearly all of them have a direct effect upon the epidermis, and some of them (chromic, osmic, and picric acids) stain it.

As decolourisers of the epidermis, the salts perchloride of mercury, ferrous sulphate, acetate of potash, &c., were found of service. They act mostly by directly affecting the horny layer.

The alkaline salts (carbonates of soda and potash, &c.) were found to be useless.

The acid salts act much in the same way as acids, though in some cases they are more useful. When they are used, the specimens must be well washed before being placed in alcohol.

Treatment with iodine, and subsequent decolorisation by alcohol, which is so commonly used in preparations of bacteria, is almost useless in the case of the epidermis. On the one hand the iodine colour sticks so fast to the epidermis that subsequent decolorisation is almost impossible, and, on the other, minute particles of the colouring matter are deposited on the surface of the horny cells, which have very much the appearance of cocci and bacilli.

Reducing agents, which have so far only played a small part in bacteriology, seem especially useful in the preparation of epidermic bacteria. They act either upon the horny substance itself, as a consequence of which the staining material is loosened and more easily dissolved, or they exert a chemical action upon the anilin dye. The process is too quick to be a reduction in the chemical sense.

Boeck found in resorcin an excellent agent. It has two properties through which epidermis is affected, and both of them may account for its decolourising power. Besides its reducing properties, resorcin, like all phenols, has the power of converting keratin into a swollen, white amorphous mass, in consequence, we may suppose, of taking up water.

Permanganate of potash alone did not act well; but, in combination with $H_2O_2$, it gave excellent results. The epidermis is almost entirely decolourised, and the bacteria show up well. Chlorate of potash and $H_2O_2$ gave equally good

results. The author then made some further experiments and found, if the specimens were dipped in a solution of common salt and then in $H_2O_2$, that, after decolourising with alcohol, the epidermic bacteria were well brought into view. He got equally good effects with ammonium chloride, and potassium iodide.

We may lay it down as a general rule that the stained epidermis is not quickly decolourised by salts and alcohol alone, or by $H_2O_2$ and alcohol alone ; the successive use of these agents, however, gives excellent results. For double-staining the epidermic fungi we possess von Sehlen's method, which consists in first staining with fuchsin, then decolourising the bacteria with acids and alcohol, and staining them with methyl-blue or gentian violets.

According to the author this method is not very satisfactory, for different parts of the sections are often differently stained, and, what is more important, some kinds of fungi are not stained at all, and consequently escape detection.

The author then goes on to give an account of twenty-four methods of decolourising preparations stained with methyl-blue, of which we may mention a few.

(16). *Sodium chloride-peroxide of hydrogen method.*—The specimens should be somewhat more deeply stained by methyl-blue than usual ; they are then placed in the salt solution (1 to 10 per cent.) for a few seconds, washed in water, passed through alcohol, placed in the $H_2O_2$ solution for five seconds, and then decolourised with absolute alcohol. They can be either mounted dry, or in oil or Canada balsam.

To show the small epidermic bacilli well, it is as well to neutralise the $H_2O_2$ solution.

(20). *Resorcin method.*—A 5 per cent. aqueous solution of resorcin is the best. The somewhat overstained specimens are left in this solution for a few seconds, and are then placed in alcohol, oil, and Canada balsam.

(18). *Permanganate of potash and peroxide of hydrogen method.*—The specimens are placed in a 1 per cent. solution of permanganate of potash, washed in water and then treated with the acid $H_2O_2$ solution of commerce. The specimens lose much of their colour, and the decolorisation is completed

with alcohol and anilin oil; then oil and Canada balsam. This method shows the large and small bacilli sharply defined and clearly.

The author gives a list of some of the best methods of staining these bacilli in a tabular series.

All specimens are first stained in the solution bora- methyl-blue āā 1, Aq. destill. 100. This he designates *B.m.b.* He gives two tables; one for sections, and one specimens obtained by pressing a small amount of the substance to be examined between two slides, much in the same way as sputum is prepared for staining.

### *Styron Method.*

| *Pressed preparations.* | *Sections.* |
|---|---|
| (1) Bmb., 1 minute. | (1) Bmb., 1 minute. |
| (2) Wash in spirit, 10 seconds. | (2) Spirit, 10 seconds. |
| (3) Decolourise in styron, 2 minutes. | (3) Styron, 4—5 minutes. |
| (4) Wash in xylol. | (4) Xylol. |
| (5) Canada balsam. | (5) Balsam. |

### *Acetic Acid Method.*

| *Preparations.* | *Sections.* |
|---|---|
| (1) Bmb., 2 minutes. | (1) Bmb., 5 minutes. |
| (2) Wash in 1 per cent. acetic acid. | (2) 1 per cent. acetic acid, 10 seconds. |
| (3) Wash in water. | (3) Alcohol absolute. |
| (4) Wash in alcohol. | (4) Oil. |
| (5) Dry over a flame. | (5) Balsam. |
| (6) Balsam. | |

### *Sodium Chloride* $H_2O_2$ *Method.*

| *Preparations.* | *Sections.* |
|---|---|
| (1) Bmb., 5 minutes. | (1) Bmb., 2 minutes. |
| (2) 1 per cent. Sod. Chlor. Sol., 5 seconds. | (2) NaCl solution, ¼ minute. |
| (3) Wash in water. | (3) $H_2O_2$ solution, 10 seconds. |
| (4) Wash in alcohol. | (4) Alcohol, absolute, 10—20 seconds. |
| (5) 3½ per cent. $H_2O_2$ solution, 5 seconds. | (5) Oil. |
| (6) Wash in alcohol. | (6) Balsam. |
| (7) Dry over flame. | |
| (8) Balsam. | |

# ON PLASMA-CELLS, ESPECIALLY IN LUPUS.[1]

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The staining methods in use for the last twenty years have almost solely demonstrated the nuclei of cells, and have left horny substance, fat, mucus, and some intercellular substances almost untouched. All those problems which concern the life of protoplasm and of the intercellular substance are still the subject of discussion, and science here comes to a full stop.

Three problems seem to block the way to further investigation.

1. "Where do the connective-tissue cells begin and where do they end?" In this question lie the boundaries of cellular pathology, and the beginning of an intercellular one.

2. The question of animal parasites in animal tissues.

3. The differentiation between protoplasm on the one hand, and the slimy material of plants on the other.

The author gives an account of various methods of staining tried by him since 1875, and then proceeds to discuss the histology of lupus. By his methods of staining protoplasm the author believes that he has settled the questions of the part that the leucocytes play in lupus, and of the origin of the epithelioid and giant-cells.

In sections of lupus large deeply-stained cells are seen, which have very much the appearance of Ehrlich's fatty granular cells. They are granular and of cubical or rhomboidal shape, but the granules are stained blue, and not

[1] "Ueber Plasmazellen, insbesondere beim Lupus."—Ärztliche Verein zu Hamburg, Marz, 1891; 'Monatsh. f. prakt. Derm.,' Bd. xii, 1891, p. 296.

violet or reddish blue, but the nucleus is also stained, thus differing from Ehrlich's cells. There is no transition from these albuminous, granular lupus-cells to the mucin-holding granular fatty cells of the same tissues. These cells are identical with Waldeyer's plasma-cells, and Waldeyer recognised them as such in some lupus sections submitted to him by the author.

These cells are the same large cells which have been recognised in lupus and tubercle and called epitheloid cells, a name which to-day is quite out of place and entirely wrong. They are found in the same situations as the epitheloid cells; they are exceedingly numerous in the most recent tubercles, and much less so in the periphery of the older ones.

The plasma-cells are the most important, as well as the earliest, part of a lupus nodule. Their formation represents the first stage of tuberculosis of the skin, and is associated with the disappearance of the collagenous and elastic tissues. It is not the endothelial cells of the capillaries, especially, which are transformed into plasma-cells; all connective-tissue cells, which are exposed to the infective virus, go through this progressive change. Nowhere do we see a transformation of leucocytes into plasma-cells.

The fate of these plasma-cells is of two kinds. They either degenerate to the central cells of the lupus nodule at once, or they undergo, before this, active proliferation. In either case they eventually become degenerated.

The large giant-cells result from the degeneration of plasma-cells. To speak accurately they are not cells at all. They consist of two parts, a degenerating and a proliferating portion. The degenerated cells enclosing degenerating collagenous or elastic fibres, and perhaps bacilli, are enclosed as a whole by neighbouring proliferating cells.

The author then goes on to speak of lupus cicatrices and states that they are not, as has been generally supposed, indifferent cicatricial tissue such as results when a simple ulcer heals. A lupus cicatrix never produces elastic tissue, and the collagenous tissues are not arranged in crossing bundles, but lie parallel to the surface of the skin.

The lupus cicatrix is histologically different from other

cicatrices, and is, in fact, lupoid tissue of remarkable durability.

If one examines the transitional stages between the tumour, consisting of plasma-cells, and the lupoid cicataix, one notices that they both pass directly into each other. The beginning as well as the end of the life of a lupus nodule (that runs a normal course) is characterised by very durable tissue, at first of an entirely cellular structure, later of a fibro-cellular one. Both, though not of the recognised structure of tubercle, in the narrower sense, are yet not less lupoid or rather tubercular than it. To many it will be a matter of opinion which tissue should be looked upon as especially tubercular. We must expect the acutest process when numerous bacilli and a rich blood-supply are present; a more chronic one with few bacilli and a meagre supply of vessels. Except in the last stages of phthisis the skin affords but a poor nidus for bacilli, and gives us in lupus an excellent picture of the primary changes of the tissues in tuberculosis. Lupus often heals without necrosis of the tissues, and gives us a very instructive, if somewhat one-sided picture of tuberculosis, and is an instance of the various effects of the tubercular poison. In the so-called surgical tuberculosis of the skin (secondary infection from underlying organs, &c.) the appearances are different—true caseation of the skin takes place from the eruption into it of a material rich in bacilli. In such cases one finds lupus tissue, but only at the edges; one finds remnants of it, or rather of the plasma-cells (the mother-tissue of every tubercle), in the surroundings of the necrotic foci in internal organs.

Koch's tuberculin acts only upon the plasma-cells; with the absorption of the plasma-cell tumour and the lupoid fibroma the action of tuberculin ceases. The degenerated, but not yet necrotic, plasma-cells are hardly affected by it.

Tuberculin has chemical affinities for the tubercular plasmoma and fibroma; it acts upon these two portions of lupus, and perhaps of all tubercle, and causes their destruction and absorption.

In conclusion, the author gives an account of some experiments he made by treating freshly excised portions of

lupus with tuberculin. He states that it does not cause necrosis of protoplasm, nor are the nuclei destroyed. Its chief action takes place in the neighbourhood of the bacilli where the giant-cells are formed.

# ON WALDEYER'S PLASMA-CELLS AND EHRLICH'S MAST-CELLS.[1]

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It appeared to be necessary from the importance of the plasma-cells in progressive disturbances of nutrition, especially in the infective granulomata, to multiply the methods of demonstrating them.

Up till now the only method in use was to stain the sections (*e.g.* of lupus) in alkaline methyl-blue (methyl-blue 1, caustic potash 0·05, water 100), and to decolourise with creosol or styron.

For general use, decolorisation by glycol is the best and most practical, as it takes place slowly.

The successive use of $H_2O_2$ and alcohol decolourises better than alcohol alone; for this purpose, however, the $H_2O_2$ solution must be neutralised.

By treating the sections with very weak alkaline solutions and then with alcohol no good results were obtained—decolourising with sodium sulpho-ichthyolicum and hydroxylaminum gave good results; the protoplasm appeared deeply stained, and the nuclei only slightly tinted.

The authors then go on to give an account of experiments they made with numerous salts, with arsenical salts, iodine, resorcin, pyrogallol, &c. They obtained the best results with resorcin, hydrochinon, and phenylhydrazin. They draw up the following scheme for the demonstration of the plasma-cells after staining with alkaline methyl-blue:

[1] "Zur Kenntniss der Waldeyerschen Plasmazellen und Ehrlichschen Mastzellen," 'Monatsh. f. prakt. Derm.,' Bd. xiii, 1891, p. 364, Dr. J. van Spek (Amsterdam) and Dr. Unna.

Decolorisation by { (1) Glycol, (2) Creosol, (3) Styron, (4) $H_2O_2$ (neutral) and Alcohol, } or by Alcohol and { Resorcin, Hydrochinon, Phenylhydrazin, Anilin,

or by acids (arsenious and osmic acids) and alcohol, or by salt (sod. chloride, soap, ichthyol, &c.) and alcohol. These methods also demonstrate Ehrlich's mast-cells very well; they are distinguishable from the plasma-cells by their reddish colour, not to mention their granular appearance, their irregular form, and their solitary position.

Sulphate of copper, carbonate of soda, arsenious acid, chrysarobin and almost all acids bring the fatty granular cells well into view. If, therefore, any doubt exists as to the nature of cells in a specimen, one has only to treat it with a dilute acid, by which procedure the plasma-cells disappear at once, while the fatty cells withstand the action of the acid for some time.

In conclusion, the authors state that they have tried a large number of combinations of decolourising methods, and can only recommend two, namely, arsenite of potash, resorcin, alcohol; and resorcin, chloride of gold (0·05 per cent.), and alcohol.

# SOME OBSERVATIONS ON RODENT ULCER.[1]

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When extirpation of rodent ulcer is impracticable, the treatment recommended by Boeck with resorcin plasters gives excellent results. The author treated a case of this disease on the lower eyelid with a 10 per cent. resorcin solution and resorcin plasters, and was astonished to find that in six months the ulcer was almost entirely healed. He states that German medical men do not seem to be able to recognise cases of this disease, for in all the cases he has seen a correct diagnosis had never been made; it is often mistaken for lupus. He considers that the disease is especially an English one; it was first described by the Irish oculist, Jacob. Histologically and clinically, it is a typical carcinoma. The author's cases occurred for the most part in sailors, or in people who had crossed the seas. In three cases he found it in conjunction with another skin disease peculiar to sailors, viz. "sailors'-skin." In this disease the epidermis covering the backs of the hands, the face, and ears becomes thickened, rough, cracked, and desquamating; and excoriations may occur and crusts form. On the face and ears localised enlargements of blood-vessels occur. The author thinks that this affection favours the development of rodent ulcer. He has found that 2 per cent. resorcin vaseline cures the "sailors'-skin."

[1] "Bermerkungen über Ulcus Rodens," 'Monatsh. f. prakt. Derm.,' Bd. xii, 1891, p. 175.

# CONTRIBUTIONS TO DERMATOLOGY

## By Dr. P. G. UNNA.

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Dr. Unna is the editor of the 'Monatshefte für praktische Dermatologie,' Hamburg and Leipzig; joint editor of the 'Atlas seltener Hautkrankheiten' (Atlas of Rare Diseases of the Skin), and of the 'Flora Dermatologica.'

# ON THE

# APPEARANCE OF HERPES ZOSTER DURING THE ADMINISTRATION OF ARSENIC.

By LUDWIG NIELSEN,
SECUNDARARZT TO THE GENERAL HOSPITAL, COPENHAGEN.

Every now and then herpes zoster appears in patients while under a longer or shorter course of treatment with arsenic.

In some of the published cases zoster has appeared during the administration of arsenic in lichen ruber: thus Hans v. Hebra[1] has noted two; Kaposi,[2] three. There are, however, other diseases where arsenic has been given and herpes zoster has made its appearance; psoriasis (Juliusburger,[3] and also two cases of lichen ruber), chorea (Bókai,[4] three cases), and nervous debility in consequence of spermatorrhœa (Epstein,[5] one case).

[1] H. v. Hebra, 'Morbid Affections of the Skin,' 1884, p. 204.

[2] Kaposi, "Remarks upon the recent outbreak of Herpes Zoster, and upon its ætiology," 'Supplement to the Archives of Dermatology and Syphilis,' 21st year, 1889, pp. 57—72 ('Transactions of the Dermatological Congress in Prague').

[3] Juliusburger, "The Appearance of Herpes Zoster during the Use of Arsenic" ('Quarterly Journal of Dermatology and Syphilis,' 1884, pp. 97—104, containing also an index of the literature on the subject).

[4] G. Bókai, jun., "Three Cases of Chorea Minor treated with arsenic; eruption of Herpes Zoster," 'Monthly Journal of Practical Dermatology,' 1889, vol. viii, p. 39.

[5] E. Epstein, "Herpes zoster, H. facialis, and H. genitalis," 'Quarterly Journal of Dermatology and Syphilis,' 1886, pp. 787, 788.

In accordance with the statements of various writers the eruption runs the usual course, it gets well, no relapse occurs in spite of the continued use of the drug, and the patients show otherwise no sign of intolerance.

The opinions of these writers as to the relation between arsenic and herpes zoster are very diverse, based as they are upon their relatively frequent coincidence. Several (Kaposi, James White, and others) regard it as accidental; so does Juliusburger, who mentions it, however, as remarkable that the patients have often been in the hospital for some months, and consequently the possibility of infection, as suggested by some, is excluded. Kopp[1] also regards it rather as an accidental coincidence, since no real proof of an interrelationship has been adduced.

Neisser,[2] who has seen a far greater number of cases of herpes zoster after the free administration of arsenic than Kaposi, is still uncertain whether any relationship subsists between the two. Lastly, some writers (H. v. Hebra, Epstein, Bókai, Hutchinson,[3] and others) admit a causal relationship between the use of arsenic and herpes zoster.

While referring to the hospital reports of the cases of psoriasis from 1864 to 1889 inclusive, we were struck by the not inconsiderable number of patients suffering from psoriasis who were attacked by herpes zoster while under the usual treatment with arsenic.

We shall now give some further particulars about these cases.

Of 777 cases of psoriasis (514 patients) observed during the above-mentioned period,[4] 557 cases (319 patients) were

[1] Kopp, 'Trophoneuroses of the Skin,' Vienna, 1886, p. 103.

[2] Neisser, 'Discussion upon Kaposi's Address,' p. 67.

[3] J. Hutchinson, "The Study of Skin Diseases as illustrating the doctrines of General Pathology," 'Brit. Med. Journal,' 1887, 23rd and 30th July, Nos. 1386 and 1387. Hutchinson's first assertion that arsenic could cause herpes was published in the 'Medical Times and Gazette' for 1868, vol. ii, p. 722, but I have not been able to refer to the volume. This was probably the earliest mention of the subject.

[4] During the period, 150 patients suffering from psoriasis were admitted in addition: these were, however, not detained more than one or two days in the skin wards. Delirium tremens developed in a few; the majority, however, were suffering from venereal disease, with which psoriasis happened

under treatment with arsenic[1] for varying duration; external treatment was also prescribed. In the remaining 220 cases iodide of potassium in large doses was administered, or external treatment alone was employed. In a very few cases other remedies (carbolic acid in pill form) were given.

In ten of the total number of cases herpes zoster appeared after a longer or shorter course of treatment, and only in those patients who were being treated with arsenic. Moreover a female patient stated that before admission to the hospital she had, while taking arsenic, just had an attack of zoster.

If this case be excluded as not coming under direct observation, 1·8 per cent. of 557 cases of psoriasis treated with arsenic suffered from an attack of zoster. Moreover it did not appear in a single one of the remaining 220 cases that were differently treated.

Again, just as herpes zoster under ordinary circumstances only very seldom attacks the same patient again, so also in these patients it appeared but once. The 557 cases represent 390 patients, therefore one in every thirty-nine patients was attacked by herpes zoster while under the influence of arsenic (2·6 per cent.).

In two patients only (*v.* Synopsis of cases, Nos. 8 and 10) the arsenic treatment was interrupted, viz. on the third and second day respectively before the appearance of the eruption. In the remaining eight it was continued during the eruption as well as after its disappearance.

The duration of the treatment with arsenic before the eruption of herpes zoster differed considerably in the ten patients. In seven the interval that elapsed was one month or more (in No. 3, three and a half months); in the remaining three, from nine (No. 9) to twenty-five days.

to be associated as a trivial complication, and it was for the former disease they sought hospital treatment. Herpes zoster appeared only in one of the 150, shortly before admission of the patient, who was suffering from chronic syphilitic disease of the brain. In none of these cases did herpes zoster appear while actually in the hospital.

[1] As arsenious acid, or as its potassium or sodium salts administered in pill form or in solution. Arsenic was only administered subcutaneously quite recently and in a small number of cases.

Unfortunately, the amount of arsenic administered cannot be stated, except in case No. 10, where $14\frac{1}{4}$ milligrams of sodium arseniate were given (about quarter of a grain). In this case (No. 10) epigastric oppression and an urticaria-like exanthem preceded the eruption of the herpes zoster; in another (No. 3), transient diarrhœa was present; in all the rest, however, no toxic symptoms were manifest.

In spite of the continued administration of the drug in the majority (8) of the patients after the eruption of herpes zoster, not one had a second attack. The same remark holds good with those patients (Nos. 1, 2, 8, and 9) who were admitted again later on (No. 1 on no less than three different occasions), and subjected again to a course of arsenic.

The cases of herpes zoster are distributed fairly evenly over this period of twenty-five years—an interval of one or two years has generally elapsed. In 1877, however, two cases appeared. Twice the interval was longer, and from November, 1869, to February, 1875 (a little over five years), no case of zoster occurred. During that time, but chiefly in 1870, a small number of patients were treated internally with carbolic acid instead of arsenic. The second long interval occurred from 1880 to 1889, when no case of zoster was seen. But from the end of 1882 to the end of 1888, of internal remedies used in the treatment of psoriasis, potassium iodide in large doses was most frequently prescribed, and only in a very small number of cases was arsenic used.

At the end of 1888 arsenic was again resumed and given hypodermically, and in the following year a case of zoster appeared amongst the patients under this treatment.

Two cases occurred in each of the months of February, March, and October, one only in April, May, September, and November. The eruption attacked 4 males, 6 females. Eight patients were between eight and twenty-two years, 2 between forty and forty-six.

As regards locality, herpes zoster dorso-pectoralis occurred seven times, herpes zoster dorso-abdominalis twice, herpes zoster lumbo-femoralis once.

The rash was always confined to one side in a few cases but slightly developed, in others fairly extensive.

On several occasions "points douloureux" were noted, but in one case only (No. 8) is general malaise stated to have been present. With all the patients the course of the affection was the usual one, as in ordinary uncomplicated cases of herpes zoster.

The psoriasis was in some cases slight, in others extensive; in one patient (No. 8) patches of psoriasis developed in the herpetic region shortly after the disappearance of the herpes zoster.

One only of the ten patients (No. 8), who had old-standing kypho-scoliosis, was being treated with wet compresses and subsequent wet rubbing. It is possible that in this case the treatment may bear an etiological relationship to herpes zoster, for the rash showed itself immediately after the wet rubbing. Moreover this was one of the patients alluded to above, where arsenic was stopped three days before the eruption appeared.

In none of the other patients were we able to demonstrate any possible ætiological factor.

Psoriasis is not considered to bear any nearer relation to herpes zoster, even by those writers who, on doubtful grounds, regard the former as nervous in origin. Just as little, so far as we know, has it ever been maintained that herpes zoster appears frequently with, or as a complication of, psoriasis. On the contrary, no herpes zoster was seen in the 220 cases which were not under arsenic treatment. Further, clinical observers have not noticed it in connection with any particular disease, and certainly not with psoriasis, but rather as a sequela of arsenic administered in very different diseases.

The relatively large number of herpes zoster cases we have brought forward—1·8 per cent. of cases, 2·6 per cent. of patients arising during the administration of arsenic, but not in any of those under different treatment (220);—in conjunction with the fact of the tolerably even distribution of the cases over twenty-five years, where the longest interval during which no zoster was seen coincided with the much less frequent use of the drug, is all the more striking, as herpes zoster is seldom seen in hospital.

Should, however, doubt be entertained in the two cases in

which arsenic was withheld two and three days respectively before the appearance of zoster—especially in the case where the rash showed itself after the cold pack—the number is still considerable. Furthermore this number does not include the case mentioned above, where the patient had just passed through an attack while taking arsenic before admission to the hospital.

Again, no comparison can be instituted between the relative frequency of the eruption after arsenic and its appearance after different treatment among hospital patients.

Lastly, the percentage of these herpes zoster cases arising in the course of arsenic treatment exceeds by far the number of patients who come to the hospital solely on account of this affection.

To illustrate this point we shall give the number of patients suffering from herpes zoster from January, 1888, to July, 1891, inclusive (my tenure of office as Secundararzt), who were treated in the skin department. Of 5267 cases of skin and venereal disease during these years herpes zoster occurred only in 14 cases (·27 per cent.). Of these, two only developed in the hospital during treatment of other diseases. In one the eruption was distributed on the nates, the patient was suffering from syphilitic paraplegia, and the eruption was regarded as the result of the spinal cord affection. The case (No. 10) was that in which the eruption occurred after hypodermic injection of arsenic.

We should also remark that arsenic was not much used during this period in other skin affections. For instance, eczema, the most frequent skin disease, was only exceptionally treated with arsenic. Pemphigus, lichen ruber, and others which are usually treated with this drug, were seldom seen here, as is the case everywhere.

The above-stated conditions admit of an overwhelming probability—in fact, prove to us—that a real relationship does subsist between arsenic and herpes zoster, although questioned and even denied by several writers. In fact, under certain though not well-known circumstances herpes zoster may make its appearance, generally after a longer rather than after a shorter period of arsenic treatment.

In other words, herpes zoster must be looked upon in

these cases as a drug-rash, although without interrupting the use of arsenic it disappears in the usual manner, and does not recur, as far as observation goes, even under a renewal of the treatment on later occasions.

In contrast to local causes (traumatism, vertebral caries, &c.) of herpes zoster, arsenic may be mentioned in ætiological connection with carbon monoxide, which has produced in certain cases of poisoning herpes zoster (Leudet, Sattler). Again, in the epidemic of herpes zoster mentioned by several writers, and especially by Kaposi, it is maintained by the latter (Weiss[1] and others) that some infective source is at work, as well as some general disturbing influence.

Kaposi himself draws a parallel between herpes zoster arising during the administration of arsenic and that seen in cases of carbon monoxide. But though he recognises this as in a measure supporting the distribution of herpes zoster on only one or a few corresponding nerve territories, and therefore as hardly harmonising with his infective theory, he nevertheless maintains it to be an accidental coincidence.

Although we believe it is as good as demonstrated from our researches that arsenic can give rise to herpes zoster, yet this does not seem to conflict with the theory of infection.

The following is a synopsis of the ten cases on which the above statements are based.[2]

[1] E. Weiss, "Epidemic Zoster," 'Archives of Dermatology and Syphilis,' 1890, p. 629.

[2] I have to thank Primararzt Professor Haslund for the patients' cases, which are considerably abbreviated, partly for want of space and partly for convenience of reference.

*Synopsis of cases given by the*

| No. | Sex, age, occupation, previous history. | Description of psoriasis. | Number of days under treatment. | Preparation of arsen and other treatm |
|---|---|---|---|---|
| I | Boy, æt. 11; psoriasis from 4 years old. | Nummularis and annularis on scalp, body, and extremities; extensive. | From March 21st to July 7th, 1864; about 3½ months. | Liquor Sodii Arse increasing doses and ointments. |
| II | Female, æt. 15, domestic servant. | Guttata and diffusa on scalp and body; fairly extensive. | From Jan. 19th to May 29th, 1866; about 4½ months. | Liquor Sodii Arse increasing doses and tar preparati |
| III | Girl, æt. 13. | Punctata and diffusa on body and extremities; fairly extensive. | From June 22nd to Oct. 31st, 1868; about 4½ months. | Liquor Sodii Arse increasing doses and tar preparati |
| IV | Boy, æt. 8. | Papularis on extremities and left ear; slight. | From Nov. 1st to Dec. 27th, 1869; nearly 2 months. | Liquor Sodii Ars baths and tar tions. |
| V | Female, æt. 15. | Guttata, nummularis, and annularis on body and extremities; fairly extensive. | From Jan. 5th to March 18th, 1875; about 2½ months. | Mistura Arsenicalis 10 to grms. 300 li baths and vario ments. |
| VI | Female, æt. 19, domestic servant. | Very extensive patches on scalp, face, body, and extremities. | From July 31st to Oct. 12th, 1877; about 2½ months. | Mistura Arsenicalis 10 to grms. 300 li baths and vario ments. |
| VII | Girl, æt. 13. | Punctata and guttata on body, extremities, and face; strongly marked. | From Aug. 9th to Oct. 5th, 1877; nearly 2 months. | Mistura Arsenicali strength as above and tar ointment |
| VIII | Male, æt. 22; several times treated; kyphoscoliosis (since æt. 10). | Guttata, nummularis, and diffusa on scalp, face, body, and extremities; strongly developed. | From Jan. 14th to June 18th, 1878; 5 months. | Mistura Arsenica above). On Ja Liq. Arsenicalis c Ferri Pomati; ba tar remedies. ( 29th arsenic stop wet pack ordered. |
| IX | Male, æt. 40; psoriasis from childhood; several times treated with arsenic. | Nummularis and diffusa on hairy scalp and extremities; fairly well developed. | From April 13th to June 10th, 1880; nearly 2 months. | Mistura Arsenica above); baths preparations. |
| X | Female, æt. 46, ship's stewardess; psoriasis from childhood. | Patches extensive and well marked. | From Feb. 13th to March 19th, 1889; 1½ months. | Sol. of Sodium A (ctgrms. 2 to gr ·5 c.c., about 9m, hypodermically; on March 10th. tions given—14¼ =¼ grain of the s |

*ıted by the Translator*].

| appearance of herpes zoster. | Description of site. | General remarks. |
|---|---|---|
| ith, *i. e.* 68 days after ıencement of arsenic. | *Right side.*—Sacral region, inner side of thigh, outer side of knee. | Under treatment 4 years previously. Arsenic also given on three distinct subsequent admissions. No zona. |
| h, *i. e.* 22 days after ıencement of arsenic. | *Left side.*—From back to umbilicus. | No recurrence of zona on treatment with arsenic on a subsequent admission. |
| ıth, *i. e.* 114 days after ıencement of arsenic. | *Left side.*—Over angle of scapula and side of thorax. | Arsenic stopped two days on account of diarrhœa (2nd to 4th July). No recurrence of zona. |
| 16th, *i. e.* 25 days after nencement of arsenic. | *Left side.*—Over crest of ilium. | No recurrence of zona. |
| th, *i. e.* 34 days after nencement of arsenic. | *Right side.*—3rd and 4th intercostal spaces from spine to sternum. | "Points douloureux" in axilla and 2nd intercostal space. No recurrence of zona. |
| th, *i. e.* 68 days after nencement of arsenic. | *Left side.*—Under the mamma. | — |
| 7th, *i. e.* 29 days after nencement of arsenic. | *Right side.* — Over shoulder-blade, in axilla, and nipple. | No painful spots and no recurrence of zona while in hospital. |
| arch 4th, *i. e.* 3 days after ping arsenic, and after g the wet pack. | *? side.* — From mid-dorsal spine, round the thorax, to ensiform cartilage. | General malaise, painful areæ over the spine and angle of scapula. On March 13th, *i. e.* 9 days later, psoriasis in herpetic region. No recurrence of zona on a subsequent admission during arsenic treatment. |
| ril 22nd, *i. e.* 9 days after nencement of arsenic. | *Right side.*—Over 6th intercostal space. | Painful area in dorsal region. Zona was not present on a previous occasion, nor any recurrence on a subsequent occasion, with arsenic treatment. |
| Iarch 9th papules, size pea, resembling urticaria, tered in groups of two and e over the body. On March 1, 2 days after arsenic was ped, zona appeared. | *Left side.* — Outside angle of scapula and below ensiform cartilage. | Epigastric oppression on day of urticaria-like eruption. Painful areæ in herpetic region. No recurrence of zoster while in the hospital. |

# A COLLECTION

OF

# DR. Louis A. DUHRING'S PAPERS

ON

# DERMATITIS HERPETIFORMIS.

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# CASE OF IMPETIGO HERPETIFORMIS.[1]

## RECOVERY.

IMPETIGO herpetiformis, first described and so named by Hebra, is a rare disease of the skin, about which but little has been written either abroad or in this country. As I have stated in the third edition of my treatise on skin diseases, it may manifest itself in a variety of forms, all having, however, certain features in common. Cases showing the several varieties of the disease have, from time to time, presented themselves to me, one of which I shall briefly describe with the following case:

Mrs. Naomi P—, aged 24, applied for advice at University Hospital, December 26th, 1882, suffering with a mixed vesicular, bullous, and pustular disease of the skin, occupying the greater portion of the general surface. The following history was obtained. She had enjoyed good health until seven months ago, when the disease of the skin made its appearance. At the time she was six months pregnant, and in average health. The eruption began upon the abdomen, but within a week the whole surface, including the hands and feet and fingers and toes, was invaded. The first lesions were wheals, which in a few days passed into vesicles and small blebs, accompanied with violent itching. The urticarial lesions soon ceased, vesicles, blebs, and pustules now appearing from day to day. The blebs possessed the peculiarity of refilling upon being opened. Many of the lesions came out as "water-blisters," and later became whitish pustules. This change was often noticeable when they refilled a second or a third time after being evacuated. The disease increased steadily in severity up to within a week of confinement. At

[1] Reprinted from the 'Medical News,' June 2nd, 1883.

times the whole surface, including even the mucous membrane of the mouth and vagina, was literally covered with lesions. They made their appearance in the form of crops every few weeks, at one time vesicles and blebs predominating, at another time vesicles and pustules, or a mixture of all three lesions. They varied in size from a pin-head to a pea, or even a walnut, and were of different shapes, most being very irregular in outline. Some were flat, others were raised, the vesicles being generally flat.

Each attack lasted about a fortnight. The distress from the itching was almost unendurable. None of the many applications used afforded any relief, and anodynes were resorted to nightly. Early in the course of the disease the nails of the fingers and toes became affected, and the hair fell out to a considerable extent. The child was born healthy at full term, four months ago. After delivery the eruption began to decrease somewhat in severity, but it has nevertheless persisted, and now presents the same general characters as at first. In fact, at no time has the type of the eruption materially changed.

The following notes were recorded at the time of the examination :—The patient is a blonde. She is tall and spare, and is evidently in poor general health ; the expression is anxious, and she is both nervous and despondent, fearing that she will never recover. She has lost weight of late. The whole surface, especially the trunk and upper extremities, is the seat of a profuse multiform eruption, characterised by vesicles, vesico-pustules, pustules, and blebs, of the most varied sizes and shapes. Many of the vesicles are extremely small—pin-point and pin-head sized. All are tense, and have a glistening glazed look. The small lesions are, as a rule, flat, and but little raised. The pustules are more variable in size, some being as large as peas, or even cherries; the blebs are in some instances as large as cherries, or even walnuts. None of the lesions show any disposition to rupture, and are in this respect distinctly herpetic. As a rule, they are not accompanied by redness of the skin, nor by marked areolæ ; often they rise from apparently sound skin. Many of the larger ones have an irregular, jagged, or stellate outline, which gives them a "puckered" appearance, similar to

that we sometimes see in herpes zoster. This peculiarity is particularly noticeable with the pustules. Vesicles, pustules, and blebs exist in all stages of evolution; vesicles are observed passing into pustules and also into blebs. Here and there vesicles and pustules are developed side by side, and owing to the fact that the latter are whitish rather than yellowish the contrast is marked.

Another peculiarity to be mentioned is the tendency all the lesions evince to group—to occur in more or less well-defined clusters. At the same time it must be stated that this does not exist in so marked a manner as in herpes zoster. For example, here and there two or three pustules are grouped, but oftener a number of vesicles are irregularly clustered, forming a patch the size of a dime or a quarter-dollar. The eruption in no instance follows the course of nerve-tracts. The extensor surfaces are more affected than the flexor. The finger-nails show two distinct transverse ridges, indicating attacks of cutaneous outbreak.

The patient was placed upon full doses of arsenical solution and wine of iron, and used locally an ointment of oleate of bismuth. The following week, new lesions still appearing, one half of the general surface was anointed three times daily with precipitated sulphur, two drachms; olive oil, two drachms; lard, one ounce. Upon the other half of the body the "liquor carbonis detergens" (an alcoholic solution of coal-tar), one part to four of water, was applied freely. Under these local remedies improvement set in at once, both seeming to act beneficially. The tarry preparation was subsequently used (full strength) upon the whole surface. A tonic saline aperient was also prescribed for daily use in connection with the iron and arsenical mixture, and under these remedies the patient made a very satisfactory recovery. Six weeks ago she regarded herself as cured, and a few weeks later passed from under observation.

# DERMATITIS HERPETIFORMIS.[1]

UNDER the name Dermatitis Herpetiformis I propose to place a number of cases of skin disease that I have encountered from time to time. These cases at present are for the most part nameless, having been regarded and diagnosed either as peculiar manifestations of one or another of the commoner and well-known diseases, as eczema, herpes, or pemphigus, or in some cases as undescribed diseases. From these remarks it will be inferred that the disease is rare, and such in a measure is the fact. At the same time I have met with a sufficient number of cases during the last fifteen years to warrant the view that the disease is worthy of a special description and a name. I first recognised the affection as being peculiar as far back as 1871, but with the few cases observed at that time was at a loss to classify or to treat them satisfactorily. Since this date I have encountered a number of other cases illustrating the same and other varieties of the disease. In the first edition (1877) of my 'Treatise on Skin Diseases' I made no allusion to the subject, for the reason that my mind was not clear as to the relation that the several cases I had encountered bore one to another, nor that they were really all merely different manifestations of the same pathological process. In the light, however, of a number of marked cases that have now been under observation for a period of years, and of others that have been more recently noted, the statement may be made that, dissimilar as they may in some cases at first sight appear, they all represent varieties of one and the same

[1] Reprinted from the 'Journal of the American Medical Association,' August 30th, 1884.

disease, for which I propose the name dermatitis herpetiformis.

In the present communication attention will be directed to the principal features of the disease, describing more particularly its symptoms and natural course. On another occasion cases illustrating the several varieties will be brought forward.

It may be premised here that dermatitis herpetiformis includes what Hebra[1] designated first "herpes impetiginiformis," and afterwards "impetigo herpetiformis;" that is to say, that the cases of Hebra constitute one of the varieties of the disease it is proposed to call dermatitis herpetiformis. And here it may be remarked that this name must not be confounded with the "dermatitis circumscripta herpetiformis" of Neumann, a term introduced by this author a few years ago to designate lichen planus, which at that time he supposed to be an undescribed disease. It may be added that this term is now no longer used by Neumann.

In the second edition of my 'Treatise on Skin Diseases' (1881), p. 276, under the title impetigo herpetiformis, will be found an abstract of Hebra's description of the disease he so named.

His account may be summarised as follows. It is a rare and grave form of skin disease, of which at the date of his report he had seen but five examples, four of which terminated fatally. The disease is characterised by the formation of yellowish pustules, arranged in groups or in an annular form, which tend to run together and to dry into yellowish, greenish, or brownish crusts, beneath which a red, excoriated, moist surface exists. On the periphery of the lesions and patches new groups and rings of pustules form. The course of the disease was similar in every case. Each outbreak of pustules was preceded by malaise, chills, fever, and systemic disturbance. The disease occupied all regions, with preference for the anterior surface of the trunk and the flexor surfaces of the thighs.

Single cases under different names[2] were before this date

[1] 'Wiener med. Wochensch.,' No. 48, 1872; see also 'Lancet,' March 23rd, 1872.

[2] 'Wiener med. Wochensch.,' No. 48, 1872; the 'Lancet,' March 23rd,

reported by Baerensprung,[1] Neumann,[2] Auspitz,[3] and Geber.[4] Heitzmann[5] has more recently also reported a case with the name impetigo herpetiformis. As supplementary to Hebra's description, I gave my own experience with hitherto undescribed varieties of the disease in the following language:—"*Within the last ten years I have from time to time met with cases, occurring in both sexes, representing other phases of the disease than heretofore described. In some cases the lesions were vesicular and bullous,*[6] *in others pustular; in still others, and in the majority of cases, bullous and pustular combined, or these lesions appearing alternately,—the disease being at one time vesicular and bullous, at another time pustular. In all instances the disposition to group or to extend about the periphery was more or less marked. A varied amount of constitutional disturbance with violent itching was always present. The disease manifested a disposition to constant recurrence, in the form of repeated attacks, extending in the majority of cases over years, and was but little influenced by treatment. None of the cases occurred in pregnant women, nor in any case has the disease proved fatal. The disease is liable to be confounded with eczema, ecthyma, and pemphigus, according as the lesions happen to be vesicles, pustules, or blebs. The ætiology and pathology of the disease are both obscure. In some cases it possesses many features in common with pemphigus; . . . . . other cases, however, manifest but little disposition to the formation of blebs. It is therefore evident that the process is capable of appearing in the form of various lesions, and that the true impetigo herpetiformis represents but one variety of the disease. More information is needed before the disease can be assigned its proper place in classification.*"

1872; 'Atlas der Hautkrankheiten,' Heft 9, Tafeln ix und x, Wien, 1876.

[1] 'Atlas der Hautkrankheiten,' Tafel viii, Berlin, 1867.

[2] 'Lehrbuch der Hautkrankheiten,' Auflage iii, Wien, 1873, p. 173.

[3] 'Archiv für Derm. und Syph.,' Heft 2, 1869, p. 246.

[4] 'Jahresb. des K. K. allg. Krankenhauses zu Wien, Jahrg. 1871.

[5] 'Archives of Dermatology,' January, 1878.

[6] In Hebra's fifth case the disease was characterised by vesicles and blebs, from which circumstance he was inclined to regard the disease as a variety of herpes, and designated it "herpes impetiginiformis" ('Lancet,' March 23rd, 1872).

These words, written four years ago, give a brief account of the disease which is the subject of this communication, and portray its important features. The description is succinct, but it embraces the leading points, and, it may be added, agrees with the views I hold at the present time.

It will be seen from this description that the name impetigo herpetiformis is altogether inappropriate to express the condition in other and equally important varieties of the disease. The cases that fell under Hebra's observation were for the most part instances of the pustular variety, and he therefore regarded the name he selected as proper; but to call a vesicular or bullous disease "impetigo," with our present ideas of nomenclature, is of course most confusing. Because of the multiformity of the lesions manifested in the several varieties which will be shown may exist, therefore I think the term dermatitis more suitable, allowing as it does all varieties of this most protean affection to come under its title. The adjective herpetiformis expresses the chief characteristic of the disease, and, as in Hebra's cases of the pustular variety, has been present in all of my cases. The disease is unquestionably herpetic, especially in its typical and commonest manifestation; that is, the lesions tend to be vesicular, and to occur in small groups or clusters. And for this reason it has on several occasions occurred to me that the affection might be regarded as a herpes, an observation that was also made by Hebra, and by the other reporters of cases mentioned. All of these observers recognised its herpetic character. The name herpes pruriginosus, it might be suggested, would seem suitable, and would answer well for most of the cases observed, itching being almost always a marked and constant symptom. At the same time if this term were adopted our present definition of herpes would require to be changed, and we should be obliged to regard pustular and bullous lesions as manifestations of herpes, an admission which would be confusing or even disastrous in its results.

For these reasons I think the name now introduced preferable. That such a protean disease as I have intimated exists, and that these varied cutaneous manifestations

are all but forms of one pathological process, there can be no doubt; and I shall elucidate this point by describing the several important varieties, which, as in the case of eczema, are based upon the predominance of certain lesions. Before doing this, however, I may refer to certain symptoms common to all forms of the disease, to which no particular allusion has as yet been made. In severe cases prodromata are usually present for several days preceding the cutaneous outbreak, consisting of malaise, constipation, febrile disturbance, chilliness, heat, or alternate hot and cold sensations. Itching is also generally present for several days before any sign of efflorescence. Even in mild cases slight systemic disorder may precede or exist with the outbreak. This latter may be gradual or sudden in its advent and development. Not infrequently it is sudden, one or another manifestation breaking out over the greater part of the general surface diffusely or in patches in the course of a few days, accompanied by severe itching or burning.

A single variety—as, for example, the erythematous or the vesicular—may appear, or several forms of lesion may exist simultaneously, constituting what may very properly be designated the multiform variety. The tendency is, in almost every instance that I have observed, to multiformity. There is, moreover, in almost every case a distinct disposition for one variety, sooner or later, to pass into some other variety; thus for the vesicular or pustular to become bullous, or *vice versâ*. This change of type may take place during the course of one attack or on the occasion of a relapse; or, as is often the case, it may not show itself until months or years afterwards. I have notes of several cases where, during a period of from two to five years, the erythematous, vesicular, and bullous varieties were all in turn manifested. Permit me, however, to state again that not only multiformity of lesion, but irregularity in the order of development, is the rule, whether during an attack or later in the course of the disease.

Itching, burning, or pricking sensations almost always exist. When the eruption is profuse they are intense, and cause the greatest suffering. As in the case of eczema, before and with each outbreak they become most violent,

abating in a measure only with the laceration or rupture of the lesions.

The disease is rare, but is of more frequent occurrence than I formerly supposed. I have encountered fifteen cases during a period of as many years, drawn from hospital, dispensary, and private practice. All, with one exception, were adults, including both sexes in about equal proportion. The natural history is interesting. The process is in almost all instances chronic, and is characterised by more or less distinctly marked exacerbations or relapses, occurring at intervals of weeks or months. The disposition to appear in successive crops, sometimes slight, at other times severe, is peculiar. Relapses are the rule, the disease in most cases extending over years, pursuing an obstinate, emphatically chronic course. All regions are liable to invasion, including both flexor and extensor surfaces, the face and scalp, elbows and knees, and palms and soles. Excoriations and pigmentation, diffuse and in localised areas, are in old cases always at hand in a marked degree. The pigmentation is usually of a mottled, dirty yellowish or brownish hue, and is persistent. I have seen it as pronounced as in chronic pediculosis corporis.

The more important forms of the disease may now be considered.

### Dermatitis Herpetiformis (Erythematosa).

The erythematous variety manifests itself in patches or as a diffuse efflorescence, as an erythema or superficial inflammation, usually of an urticarial or erythema-multiforme-like type. The urticarial element may be marked, the skin showing a disposition to acute œdematous infiltration in a diffuse form. Urticarial complication, rather than urticaria, is suggested by the condition of the skin; in like manner, a resemblance to diffuse erythema multiforme may be noted. At times the patches, whether discrete or confluent, are circumscribed; and later, by their coalition, show irregularly-shaped, marginate outlines, as in erythema multiforme. The colour varies with the shape, being at first

bright red, but soon becoming deep red or violaceous, mottled, and tinged with yellowish hues. The variegation is usually pronounced in the later stages of the process, at which period more or less diffuse pigmentation is also present. Together with the erythematous inflammation there may form maculo-papules, or circumscribed or diffuse flat infiltrations, variable as to size and shape; also vesico-papules, the process now bearing a resemblance to the first stage of herpes iris. It will thus be noted that the eruption, in its general aspect and course, is much like that of erythema multiforme. In severe cases the outbreak is preceded by and accompanied with malaise, chilliness, or slight febrile disturbance. The itching is generally violent, the disease differing in this respect from erythema multiforme.

Its course is variable. It may continue for days or weeks, or, as is usually the case, it may pass into the multiform variety, to be described later. It may be the first manifestation, or it may follow other varieties as a relapse.

As a variety it is not as clearly defined as the vesicular, bullous, or pustular, in some cases it appearing to be but the first manifestation of one of the first-mentioned forms. But it is important that its features be described, for the reason that it is liable to be met with as a clinical picture, and may readily be confounded with other diseases, notably urticaria, erythema multiforme, and eczema. I recall two cases where the diagnosis was at first difficult, and it was not until other manifestations appeared on the skin that the true nature of the process became evident.

### Dermatitis Herpetiformis (Vesiculosa).

The vesicular variety is that most frequently met with. It is characterised by variously sized, varying from a pin-head to a pea, flat or raised, irregularly shaped or stellate, glistening, pale yellowish or pearly, usually firm or tensely distended vesicles, as a rule unaccompanied by areolæ. In their early stages they can be seen only with difficulty, and are liable to be overlooked in the examination. Some-

times they can only be detected or seen to advantage in an oblique light. This observation I have repeatedly noted, and it arises from the fact of the lesions being flat, translucent, and without areolæ. In size they vary extremely, large and small being formed side by side, and in this respect they differ from the vesicles of eczema. Here and there papules, papulo-vesicles, vesico-pustules, and small blebs will sometimes be encountered. Concerning their distribution, the eruption as a whole is disseminate, the lesions existing scattered more or less profusely over a given region, as, for example, the neck or the back, but they are for the most part aggregated in the form of small clusters or groups of two, three, or more; or there may be patches here and there as large as a silver dollar, upon which a number will be seated. When in close proximity they incline to coalesce, as in herpes zoster, forming multilocular vesicles or small blebs. Where this occurs they are generally slightly raised, and are surrounded with a pale or distinctly reddish areola, which shows forth the irregular, angular, or stellate outline of the lesion. At this stage, moreover, the little cluster will generally present a "puckered" or "drawn-up" appearance, indicative of its herpetic nature.

The eruption is usually profuse, sometimes to the extent of the upper extremities, trunk, and thighs being well covered. It may attack any region, the neck, chest, back, abdomen, upper extremities, and thighs, all being especially liable to invasion.

The most striking symptom is the itching. Not infrequently burning is also complained of. Itching, however, predominates, and is in all cases violent or even intense. Patients state that it is altogether disproportionately in excess of the amount of eruption. It is, moreover, a persistent itching, causing the sufferer to scratch constantly. It generally precedes the outbreak, and does not abate until the lesions have been ruptured. Old sufferers, familiar with the natural course of the process, have informed me that they can obtain no relief until the lesions have been ruptured. From my observation I should say that the itching was both more severe and more lasting than in vesicular eczema. The vesicles make their appearance slowly, so that several

days or a week may be required for their complete development. Notwithstanding that scratching is indulged in in the early stages of the disease, excoriations are not prominent, owing to the fact that the walls of the lesions are tough, and do not rupture, and that they incline to refill immediately on being evacuated.

The diagnosis in some cases is attended with difficulty, on account of the resemblance to vesicular eczema. I recall the embarrassment experienced in the classification of the earlier cases encountered, and the provisional diagnoses of "vesicular eczema?" made at the time. But the irregularity in the size and form of the vesicles; their angular or stellate outline; their firm, tense walls, with no disposition to rupture, and their herpetic character, will all serve to aid in the diagnosis. In some cases the constitutional disturbance and the magnitude of the eruption, as regards profusion, distribution, and multiformity, showing a more formidable disease than eczema, will also be striking. The itching and burning will usually be found to be more continuous and intenser than in eczema. The obstinacy of the disease to the ordinary treatment of eczema, moreover, must also soon become apparent, the usual milder remedies so frequently of service in acute vesicular eczema being of little or no benefit in this disease. Finally, the tendency to repeated relapses, and the chronicity of the affection, must strike the observer as peculiar. This variety cannot be confounded with herpes zoster, herpes iris, or pemphigus. Its relations to the "herpes gestationis" of some authors will not be considered in this paper, further than to state that in my opinion they are probably one and the same disease. On a future occasion I shall deal more at length with this point.

### Dermatitis Herpetiformis (Bullosa).

In the bullous variety the lesions are more or less typical blebs, tense or flaccid, rounded or flat, usually the former, filled with a serous or cloudy fluid, seated upon a non-inflammatory or slightly inflamed base. In size they vary

from a pea to a cherry or walnut, and are for the most part irregular or angular in outline. They incline to group in clusters of two or three, the skin between them in this event being reddish and puckered. Sometimes in immediate proximity—almost contiguous—will exist one, two, or three, or a part of a circle of small, pin-head sized, flat, whitish pustules. Vesicles of all sizes, flat or raised, are also generally found near by, or disseminated over the affected surface. As in the other varieties, all regions may be attacked, especially the trunk, upper extremities, and thighs. In several cases I have seen the greater part of the general surface invaded most profusely, in which event the lesions are usually smaller than where comparatively few exist. They incline to appear in crops at irregular intervals, as in the other varieties. The lesions are generally ruptured in the course of a few days, and then crust over with a yellowish, greenish, or brownish crust. They are accompanied by burning and itching, which may be very severe. They bear resemblance to those of pemphigus vulgaris, with which of course they may be readily confounded, but they are more herpetic in character. They differ in that they incline to group, and have a more inflammatory herpetic aspect, the type of which picture is seen in herpes zoster. Moreover around and near the bleb will usually be found vesicles and pustules, the latter often in close proximity, the whole manifestation being quite different from that of pemphigus.

### Dermatitis Herpetiformis (Pustulosa).

The pustular variety is generally less clearly defined than the vesicular, because the lesions are often intermingled with vesicles, vesico-pustules, and blebs. In typical cases the pustules are acuminate, rounded or flat, tense or flaccid, usually the former, and vary in size from a pin-point to a pea or silver quarter-dollar. Vesicles and blebs in some cases precede the pustules. The smallest lesions are generally flat, or on a level with the surrounding skin, and, as stated, are frequently not larger than a pin-point or pin-head. Larger pustules, the size of a pea, are generally

rounded or acuminate, and are surrounded by a reddish inflammatory areola. Later they incline to flatten, and to increase in size by spreading peripherally, and drying in the centre.

Sometimes they are seated on a slightly raised base. When fully matured they generally present an "angry" appearance, the skin immediately around them having a "puckered" look, from the fact that the pustule itself is irregular in outline, as sometimes is the case in herpes zoster.

They incline to form in groups of two, three, or more, and, moreover, often appear in patches of two or more groups. Such an arrangement is generally met with on the trunk. The grouping is further peculiar in that a central pustule will often be immediately surrounded by a variable number of smaller pustules, sometimes in a circinate form, as in herpes iris.

In other localities, however, no such peculiarity occurs, the lesions being discrete, and even disseminate. The pustules are usually opaque, and of a whitish colour; sometimes they are yellowish, though they are seldom so yellow as in pustular eczema. Not infrequently slight hæmorrhagic exudation occurs, as in the later stages of herpes zoster, giving them a reddish, bluish, or brownish hue. They are generally accompanied by sensations of heat, pricking, or itching; in some cases these symptoms precede for several days the eruption. They pursue a slow course, from one to two weeks being usually necessary for their full development; in other cases their maturation occurs more rapidly. In some cases, together with the pustules are found vesicles and blebs of various shapes and sizes, and these often form immediately by the side of, or in close proximity to, the pustules. Papules and papulo-vesicles may also be present. In a given area, say of a few square inches—as, for example, upon the abdomen—there may exist all of these lesions in various stages of evolution. This multiformity is striking, and presents a curious and peculiar mixture of lesions. The attacks last from two to four weeks, after which there generally follows a comparative respite of from one to six weeks. The disease may thus be

kept up indefinitely, the outbreaks being at one time slight, at another time severe.

Sometimes it has preceded other varieties ; in other cases it has followed the bullous variety ; while in some instances that have been under observation for a long period it has at intervals of months alternated between the vesicular and bullous varieties. After what has been previously said, it need scarcely be stated that this variety is identical with the "impetigo herpetiformis" of Hebra, although in but few of the cases observed by me have the symptoms been so pronounced as in Hebra's experience, if I may judge from the portraits in his Atlas of Skin Diseases. The account given by me relates to the disease as I have encountered it. Hebra's account has been already given, and need not be repeated here. The difference of experience concerns chiefly the severity of the process. Thus in none of my cases has it proved fatal, while it will be remembered four out of five of Hebra's cases died, and, according to Kaposi[1] (Hebra's successor), ten out of eleven cases observed by him have perished. Finally, I have observed it to occur about as often in men as in women, and also in the latter apart from pregnancy. Hebra, on the other hand, met with it only in women, and, moreover, only during the parturient state.

Concerning the constitutional symptoms, they may be stated to vary with the gravity of the attack. Usually, however, they are more marked than in the other varieties, rigors and alternate paroxysms of heat and cold being especially noticeable. It is the most serious phase of the disease.

### Dermatitis Herpetiformis (Papulosa).

The papular variety is in my experience rarer than any other form. I have met with only two cases, one in an adult, the other in a boy, and in both of these the eruption was scanty. It is characterised by the formation of small or large pea-sized, irregularly-shaped, usually firm, reddish

[1] 'Pathologie und Therapie der Hautkrankheiten,' 2te Auflage, Wien, 1883.

or violaceous papular lesions, occurring for the most part in groups of two or three, scattered here and there over the affected surface. They are of variable size, large and small ones not infrequently existing side by side, and are as a rule ill-defined, being neither acuminate nor flat, but resemble the papular infiltrations sometimes met with in abortive herpes zoster. They are of an acute or subacute inflammatory type, and, as stated, bear resemblance to abortive herpetic lesions, and also to certain phases of chronic relapsing papular eczema. Their surfaces are generally excoriated from scratching, and may be covered with blood-crusts, or with slight, adherent, thin epidermic scales.

The itching is severe, so much so that comparatively few lesions may so torment the patient as to interfere with the night's rest.

Ill-defined papulo-vesicles are also met with here and there, as in the case sometimes of papular eczema. The lesions pursue a slow, chronic course, lasting from one to two or four weeks, when they gradually disappear, leaving more or less pigmentation. Relapses are the rule at longer or shorter intervals.

As I have intimated, this variety bears a close resemblance to chronic papular eczema, and the earlier cases encountered by me were so diagnosed; but the irregularity in the size and form of the lesions, the disposition to group, the usually slow evolution of the lesions, the tendency to appear in crops at irregular intervals, the chronicity of the process, and the extreme obstinacy to local and internal treatment are all peculiar. It is the mildest phase of the disease.

### Dermatitis Herpetiformis (Multiformis).

This may be regarded in the light of clinical variety, one that is eminently useful from a practical standpoint. It is a variety of the disease in the same sense that eczema rubrum is a variety of eczema. It is important to consider it for the reason that it is a picture which may at any time show itself in the course of the disease. It is a phase not infrequently met with, and on account of the great mixture

of lesions, and the difficulties presented in diagnosis, is worthy of special description. The multiform variety consists of erythematous, sometimes slightly raised, urticarial patches of variable size and outline, often confluent, of a reddish or violaceous, yellowish, dusky, sometimes variegated colour, not unlike that of erythema multiforme. In addition there often exist more or less well-defined, irregularly-shaped or rounded maculo-papules and flat infiltrations, papules and vesico-papules, all in various stages of evolution. Small blebs and pustules, pin-point sized or larger, may also be present, though with the vesicular element predominating it is not usual to meet blebs or pustules of large size nor in numbers. As the disease is in an early or late stage of its existence will pigmentation and excoriations be slight or marked. Briefly, then, to recapitulate, there exists a mixture of lesions, with no single type predominating, calling to mind in its behaviour eczema, although it is far more capricious and protean. It must also be remembered that the process may at any period change its type, such an occurrence usually taking place with an exacerbation or a relapse. Thus the vesicular variety may exist for a variable period, to be followed in a few weeks or months by an attack of blebs, or it may be pustules, or by a mixture of the blebs and pustules. This mingling of several varieties is a marked and peculiar feature of the disease, giving a very striking dermatological picture, different from that seen in any other disease of the skin.

In conclusion, permit me to summarise by saying that I have endeavoured to show—

1. The existence of a distinct, well-defined, rare, serious, inflammatory disease of the skin, manifestly of an herpetic nature, characterised by systemic disturbance, a great variety of primary lesions, by severe itching and burning, and by a disposition to appear in repeated successive outbreaks.

2. That the disease is capable of exhibiting itself in many forms, all having a tendency to run into or to succeed one another irregularly in the natural course of the process.

3. The principal varieties are the erythematous, papular, vesicular, bullous, and pustular, which may occur singly or in various combinations.

4. That it is a remarkably protean disease.

5. That the pustular variety is the same manifestation as the disease described by Hebra under the name "impetigo herpetiformis," this being the only form hitherto described.

6. That the several other and equally important forms are worthy of special remark.

7. That the term "dermatitis herpetiformis" is sufficiently comprehensive and appropriate to include all varieties of the process.

8. That it may occur in both sexes, and in women independent of pregnancy.

9. That it usually pursues a chronic, variable course, often lasting years, and is exceedingly rebellious to treatment.

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## NOTES

OF A

# CASE OF DERMATITIS HERPETIFORMIS,

### EXTENDING OVER ELEVEN YEARS,

*Illustrating the Several Varieties of the Disease.*[1]

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In the following case the pustular, vesicular, bullous, and papular manifestations of the disease[2] were all developed on one or on several occasions during the long period the patient was under my observation. The characteristic fea-

[1] Reprinted from the 'Philadelphia Medical Times' for July 12th, 1884.

[2] For an accounnt of dermatitis herpetiformis the reader is referred to my paper read before the American Medical Association, May 6th, 1884, abstracts of which may be found in 'New York Medical Journal,' p. 562, May 17th, 1884, and in 'Philadelphia Medical Times,' p. 603, May 17th, 1884.

tures of the affection are clearly defined in the history, the notes of which, it may be remarked, were recorded at the time of each examination.

James W—, æt. 38, a native of Philadelphia, and a wood-carver by occupation, was admitted to the Philadelphia Dispensary for Skin Diseases, January 16th, 1873. According to the notes in the record-book, he was suffering from an imperfectly defined inflammatory, multiform eruption, composed of erythematous spots and patches which had evidently been the seat of previous disease, papulo-vesicles, pustules, and excoriations. It occupied the general surface, with preference for the arms and forearms, sacral region, buttocks, and thighs. The lesions were not very numerous, and were disseminated, except over the sacral region, where a dozen or more formed a conspicuous patch. The disease appeared to be fading away, and, inasmuch as the patient gave a history of having recently had quite active treatment, internal as well as external, and that he had been treated for supposed "secondary syphilis," the diagnosis was for the time being withheld. According to a note, the eruption resembled that resulting from the internal use of the iodide or the bromide of potassium.

He stated that he had been suffering from the disease for five years, and that while better, and even nearly well at times, it had never entirely left him; it was the source of great annoyance to him, itched considerably, manifested itself in different forms from time to time, and was apt to appear in distinct crops from week to week or month to month. He was not aware that he had ever contracted syphilis, but several physicians had assured him that the present eruption was a manifestation of this malady.

He was placed upon a simple tonic treatment until the diagnosis might be more definitely ascertained.

January 25th.—New pustular lesions have appeared on the buttocks and on the thighs. These are highly inflammatory, flat, and incline to crust in the centre and to spread on the circumference. Alkaline lotions and baths were ordered; also a saline aperient.

February 8th.—Considerable improvement, the disease

being in about the same state as when the patient first came under observation.

12th.—New lesions are appearing.

19th.—The disease has been manifesting itself chiefly on the arms and on the buttocks, new pustules making their appearance from day to day.

24th.—No new lesions; condition decidedly better.

March 19th.—There has been steady improvement since last note. The remedies used during the past two months have been syrup of the iodide of iron, bitartrate of potassium from time to time, and a carbolic acid lotion.

May 12th.—The disease continued improving during the last two months until within the present week, when a crop of new pustular lesions began to appear, scattered here and there over the general surface, especially upon the arms, buttocks, and thighs. The patient enjoys average general health notwithstanding the eruption, which now is abundant, and is unusually active.

It may be described in its present state as a pustular form of disease, the lesions beginning as pin-head and split-pea sized, flat *pustules*, with extensive bright red areolæ. They increase rather slowly in size, and soon begin to crust over with a yellowish-brown crust, after which they continue to increase in size by new, small, flat, pin-head sized pustules forming on the periphery. This process goes on until the lesions assume the size of a dime or quarter-dollar, when it ceases, and a crust covering the whole remains. The crust is adherent from the beginning; if detached, it shows a circumscribed, superficially excoriated surface, covered with a puriform fluid. Later, at the end of two or three weeks, the crust drops off, leaving a dark red infiltrated spot, but no scar. These inflammatory infiltrations are slow to disappear, weeks being necessary for the larger ones to become effaced.

About the buttocks and sacral region and on the thighs the lesions show a disposition to occur in patches, and, moreover, to group, two or three not infrequently existing in such close proximity as ultimately to run together. Over the arms and elsewhere this tendency is not so noticeable; nor are the lesions here so well defined and large as on the back and thighs.

26th.—The outbreak was at its height when the last note was recorded, since which date the eruption has been steadily declining.

November 3rd.—The patient has absented himself for six months. He states that he continued to improve through the summer, and that only within the last two months has the disease again become annoying. He was almost free from eruption at one period during the summer. Lately the disease has manifested itself in another form, the lesions being decidedly papular rather than pustular, and in distribution more scattered than formerly, and also much more itchy. Upon examination the eruption was seen to have changed its character completely, and to consist of disseminated, here and there distinctly grouped, variously sized and shaped, imperfectly formed *papules* and *papulo-vesicles*, which closely resembled eczema. He was again placed upon a preparation of iron and a saline aperient, the bowels being habitually constipated.

18th.—The eruption has entirely disappeared, leaving the skin pigmented in dirty yellowish-brownish spots and patches, and in some places deprived of the normal pigment, dirty whitish patches existing.

March 3rd, 1874.—Four months have elapsed since the last note. The disease has during this period been "better and worse." There have been several relapses, which have continued a fortnight or longer and have disappeared as before. The patient has taken arsenic in the form of Liq. Potass. Arsenit. in from two- to four-minim doses, but without benefit. Of late he has been using strong drink in excess, which, he states, is pretty sure to cause an exacerbation of the eruption. A new crop of lesions is to-day making its appearance. The character of the disease has again changed, the lesions now being *vesicular* and *pustular*, especially the latter, similar to the form of eruption that existed a year ago. The single lesions resemble ecthyma, while those in groups or patches bear a close resemblance to pustular eczema.

13th.—New lesions are here and there manifesting themselves, the neck, lower portion of the back, buttocks, thighs, and arms being the regions chiefly invaded. Iron and

arsenic are still being taken, and various antipruritic lotions and ointments have been employed, with, however, but little benefit.

April 3rd.—The pustular character of the eruption has ceased, and variously sized herpetic *vesicles* and small *blebs* have lately developed. Many of them are as large as split peas. They appear quite suddenly and are very itchy. The disease has lately attacked the folds of the axilla and the pubes, which regions have become extensively crusted.

24th.—The surface has again cleared off, only a trace of the former eruption remaining in the form of primary lesions; but scratch-marks and pigmentation are everywhere present, the whole integument having a dirty, muddy, mottled look. Has been taking arsenic steadily; general health has remained good.

April 30th, 1877.—Three years have elapsed since last note, and since the patient has been seen. The disease still exists, with the same history as formerly, the lesions being variable, papules, pustules, and vesicles occurring from time to time. During the past six weeks there have been several slight relapses, and again a change in the character of the lesions, indistinctly defined, flat, variously sized and shaped *papules* appearing together, with here and there ill-defined abortive *pustules* and *papulo-pustules*. These lesions now exist. The patient considers himself, upon the whole, considerably improved. He has been taking the arsenic from time to time, in varying quantity, from one to five minims thrice daily.

January 15th, 1879.—A year and a half has passed since the patient was last examined. He states that he has but little change to report. He has not been free of the eruption, and has had two very severe attacks and many slight ones. The severer attacks have continued three or four weeks, while the lighter ones come and go from week to week. He has had the eruption so constantly of late that no particular note has been made as to the occurrence of distinct outbreaks. The lesions have been coming and going without intermission. Within the year the lesions have been for the most part *vesicular* and *bullous*; or, as he expresses it, "they have been blisters of various sizes, con-

taining a clear fluid." They have had a disposition to cluster, but there have also been many isolated single lesions. They have been very itchy, so much so that he lost no time in scratching and rupturing them. He does not know whether they ever ruptured spontaneously, for he has invariably opened them as soon as they appeared. Lately all regions of the surface, except the palms and soles, have been attacked, the scalp even being the seat of numerous lesions, but preference is still shown for the regions before invaded.

March 2nd, 1879.—During the past two months he has been better than usual, the most annoyance being due to considerable eruption, vesico-pustular in character, about the scrotum. He has been drinking of late, with the hope, he states, of "bringing out the disease," but thus far without success. He has been better this winter than during any period within the past ten years. He is positive that the various forms of treatment employed have had little or no influence in controlling the disease. He is about as free of the eruption in summer as in winter, the seasons exerting no special influence upon his condition. His general health remains fair, although, owing to his irregular mode of life, he is dyspeptic, and, as a rule, is constipated.

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## A CASE OF DERMATITIS HERPETIFORMIS (*BULLOSA*).[1]

On February 3rd, 1879, the patient, the notes of whose case are about to be given, was sent to me by Dr. H. G. M. Kollock, of Newark, Del., who in his letter stated that the disease was regarded as pemphigus. The man had been under treatment for some months, during which period he had taken quinine, iron, and arsenic, and had used varied remedies locally, all without relief. Dr. Kollock's letter

[1] Reprinted from the 'New York Medical Journal' for July 19th, 1884.

states: "He has not had a full crop of bullæ for about two weeks, prior to which they would appear in great numbers every two or three days. He has never been entirely free from them."

The patient, Newton B. E— by name, was admitted to the University Hospital, at which date the following record was made:—He is sixty years of age, tall and slender, somewhat emaciated, debilitated, and nervous; he is a native of Delaware, a shoemaker by occupation, and is married. There is no special family history. He never suffered any disease of the skin, except occasional attacks of inflammation from poison ivy, until eight months ago, when the present disease appeared. He was at the time in average health, and could attribute the outbreak to no cause. It began about the ankles and feet with swelling, heat, and violent itching; the following day eruption manifested itself on the arms and around the neck, and later on the trunk. Several household remedies were applied, but the disease spread until at the end of a week he was well covered with a mixed eruption consisting of papules, vesicles, and blebs, the latter predominating, and some being as large as a walnut. Upon bursting or being ruptured, the walls adhered to the skin and formed crusts. Successive crops of blebs continued to appear until a fortnight ago—in all, during a period of eight months. He has lost flesh—as much, he thinks, as fifty pounds. A new outbreak of eruption is now manifesting itself.

*Present condition.*—The disease of the skin is almost universal, involving the greater part of the general surface from the scalp to the soles of the feet. It is made up of variously sized and shaped *vesicles, blebs,* and *pustules,* in all stages of evolution.

The vesicles predominate, and vary in size from a pin-head to a pea, the majority being as large as small peas. They are notable for their irregularity of shape, being for the most part very irregular, and in many instances angular in outline. Some are raised to the height of a line, others are flat. They are distended, and have a glistening, glazed look, and, as a rule, are not surrounded by any areola, rising abruptly from the surrounding healthy skin. They are

yellowish and contain serous contents, as in the case of the early stage of herpes zoster.

The blebs, some raised, others inclining to flatten, are met with here and there on the neck, arms, thorax, abdomen, thighs, legs, feet, and hands. Some are as large as a pigeon's egg. They are manifestly advanced stages of the vesicles, or at least often grow from these lesions. They are as a rule tensely distended, and have clear contents; some show cloudy contents and are flaccid. They do not rupture spontaneously. Their contents are alkaline.

The pustules are present in like manner here and there, distributed over the same regions. They are distinctly pustular, having *whitish* contents and more or less inflammatory areolæ; are small, raised, irregular in outline, though less so than in the case of the vesicles, and have a "puckered" or "drawn-up" appearance. Excoriations and blood-crusts are conspicuous, and are plainly the result of prolonged scratching. Yellowish, brownish, "dirty-looking" patches of pigmentation, giving the skin the appearance of chronic pediculosis corporis, are also prominent symptoms. *The itching and burning are most distressing.* They interfere with sleep at night. New lesions in great numbers are beginning to form. Some of the earliest are flat *papulo-vesicles.* They can be felt with the finger as small circumscribed infiltrations even before they become visible. In some localities there is a marked tendency for all the lesions to group, two, three, or four being crowded together into a cluster; in other places they are disseminated. Here and there *blebs* are surrounded concentrically by a variable number of small, flat, whitish pustules of the size of pin-heads, making a striking combination.

February 7th.—During the last three days lesions of all kinds have appeared, accompanied by intense itching and burning. Some of the blebs have attained the size of walnuts. On the forehead an abundant crop of variously sized and shaped herpetic vesicles are present.

28th.—A fortnight ago the attack was at its height, vesicles, blebs, and pustules, as well as intermediate forms, existing in profusion. Almost the whole integument was invaded, scarcely a square inch being exempt. The blebs

frequently reached the size of a hen's egg; the pustules flattened, seldom exceeding the size of a dime or a quarter-dollar. They spread peripherally, inclining to dry and crust in the centre. The course of both these lesions was rapid, disappearing in four or eight days, followed by crusting and pigmentation.

The general condition remained fair, there being no marked febrile disturbance, although the appetite was impaired, and the patient was weak, nervous, and much distressed in mind and body. With the cessation of new lesions the itching and burning declined, but did not leave entirely. The treatment consisted of a generous diet, with saline laxatives and small doses of arsenic and strychnia, together with antipruritic lotions of carbolic acid and tar. The man remained in the hospital several weeks longer, during which time he improved with remarkable rapidity. I cannot, however, attribute the recovery altogether to the remedies used, knowing well as we do the singularly arbitrary course the disease usually pursues.

About three years afterward (December 20th, 1882) I received a letter from Dr. Kollock (under whose care the patient had since been), stating that he had not seen the man for a year, but that, "according to last accounts, he had improved markedly in general health as well as locally under a tonic treatment. The eruption has appeared at longer intervals, and is confined to smaller areas. He seemed to derive great relief from the application of a lotion containing corrosive sublimate and alcohol." Since this date I have heard nothing.

The case represents more particularly the bullous variety of the disease, although its multiformity, as in almost all instances, was repeatedly shown. As I have so recently described this remarkable disease in a paper[1] read before the American Medical Association, comment here is scarcely necessary. It may be stated, however, that the case illustrates the vesicular and bullous lesions as they usually occur in the course of the disease, the latter predominating. The

[1] Abstracts may be found in the 'N. Y. Med. Journ.,' May 17th, 1884, p. 562, and in the 'Philad. Med. Times,' May 17th, 1884, p. 603.

resemblance to pemphigus is obvious, but I think it will be seen that the process is different, and that it cannot be viewed as a variety of this disease.

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## CASE OF DERMATITIS HERPETIFORMIS

### (*MULTIFORMIS*),

### AGGRAVATED BY PREGNANCY AND IRREGULAR MENSTRUATION.[1]

Mrs. M—, æt. 28, a resident of St. Paul, Minn., consulted me February 3rd, 1883, for a chronic inflammatory disease of the skin, involving the entire surface. She was of spare frame, with brown hair, and of a nervous temperament. She gave the following clear and interesting history of her case :—Her ill-health began three and a half years ago, up to which date she had been in good general health; had menstruated regularly and normally, and had weighed one hundred and thirty-five pounds. She had borne a healthy child three years before, without difficulty. The first manifestations were upon the tongue and in the throat, in the form of whitish spots, similar to so-called "canker-sores," which continued for six months, desquamating from time to time, the mouth being so sore and sensitive as to render eating painful. She was in the third month of her second pregnancy when the first sign of cutaneous disease appeared on the flexor surfaces of the right arm and thigh, and on the abdomen, in the form of small annular clusters of *vesicles*, occupying the space of a five-cent silver piece. The lesions were itchy from the beginning. They spread slowly, new "little water-blisters" coming out from day to day. This process progressed for six weeks, when the body was well covered with eruption, and she was com-

[1] Reprinted from the 'Medical News,' July 19th, 1884.

pelled to remain in bed. Three weeks after the attack began *blebs* appeared, accompanied by comparatively slight itching. They ruptured easily and left excoriated surfaces. As gestation proceeded the disease became steadily worse, being at its height during the fourth and fifth months, at which date *vesicles* and *blebs* of all sizes were very numerous, and the itching intense, accompanied by extensive excoriations and scratch-marks, with more or less oozing and crusting. No treatment used seemed to have any effect in relieving the symptoms.

At this date very curious lesions were noticed on the wrists and on the palms and soles. They were elongate (about an inch in length), rounded (about an eighth of an inch in thickness), firm, whitish, striated elevations, situated transversely on the wrists, the same condition existing on the palms and soles. When opened a non-offensive, cheesy mass "popped out," to use the words of the patient. The contents were not expressed, but were forced out naturally. The lesions were opened every day for several weeks, when they ceased appearing.

At the sixth month of pregnancy the skin cleared off, the lesions disappearing except a large bedsore, which did not heal until a month after delivery. The skin remained comparatively clear about one week, when small pin-head sized *vesicles*, soon followed by large hazel-nut sized *blebs*, again appeared. This crop also manifested itself on the legs and feet, regions hitherto exempt. The blebs were all large, very abundant, crowded one another, and were very itchy. Some of the lesions became pustular. Three or four weeks before delivery the whole integument became œdematous, swelled, or "puffed up," as she expressed it. This condition gradually subsided a week or ten days after the birth of the child, which was born healthy at full term, but lived only four days.

After delivery, and for three weeks following, the vesicles and blebs became fewer, the skin becoming again entirely clear of eruption, and she regarded herself as cured. She remained free, however, only a few days, when small *pustules*, pin-point in size, appeared in abundance; these disappeared and were followed by a crop of mixed lesions—of *pustules*

and *blebs*. This condition continued better and worse during the winter, the disease towards summer locating itself chiefly about the axillæ and groins, characterised now by an offensive, excoriated, at times weeping, crusted surface, with itching. Through the summer the skin of the palms and soles thickened, beneath which pus formed, undermining it. This continued for three or four months.

In August, 1881, she indulged in a bath, just before the menstrual epoch, after which the face became blotchy, bluish, and swollen, giving her "a dissipated look." Vapour-baths taken repeatedly for one month completely exhausted her. September 1st the menses failed to appear, and October 1st there was a slight discharge, at which date she again broke out with variously sized *vesicles* and *blebs*, the latter for the most part as large as a hazel-nut, many of them having puriform contents. There was now much excoriation and crusting, the bed-linen everywhere adhering to the raw skin. Numerous small, pin-point sized *vesicles*, closely crowding one another, again came out over the whole surface. They were so abundant that a pin-point could scarcely be put down between them. She was "literally covered with them," and this condition, in the form of crops, lasted all winter.

The skin disease later again changed its character, large *blebs* and *pustules* appearing, especially upon the face, which was much swollen.

The menstrual flow remained absent five months (from October, 1881, to February, 1882). Arsenic in large doses, and later electricity were used, and it was thought that she was benefited by the latter. Improvement continued slowly but steadily up to July, 1882, when suddenly, and without apparent cause, violent inflammation of the hands and feet, with large *pustules* on the palms and soles and on the face, manifested itself. These continued to appear and to disappear in crops through the summer and autumn up to the present date; the lesions being as a rule shot-sized, whitish *pustules* and *vesicles*, closely crowded together over almost the entire cutaneous surface. Her general condition has been variable. On many occasions she has felt ill, weak, very nervous, depressed, with chilly or heated sensations or rigors. On one occasion the tongue swelled and became coated with

a puriform exudation with profuse salivation. Menstruation when present is usually normal. Her weight now is about ninety-five pounds (forty pounds below her former average). The appetite has always remained good. She has been under the care of a skilful specialist in skin diseases for six months, but has failed to receive any benefit.

The present condition (February 3rd, 1883) is as follows:— The whole general surface is the seat of a subacute and chronic inflammatory *erythematous* (somewhat urticarial), *papular*, *papulo-vesicular*, *vesicular*, and *pustular* eruption, the lesions being very markedly multiform. They are pin-point, pin-head, and pea sized; are thickly studded; are firm and have a shotty feel, as in the early stage of variola. The skin is everywhere much thickened, and is even tough and leathery, and is markedly pigmented, being of a mottled, reddish, dirty yellowish-brownish hue. The eruption is *intensely itchy*. The face and scalp are least affected, but, as stated, the rest of the general surface, including the palms and soles, is well covered with primary and secondary lesions.

The patient was ordered for local use an ointment of precipitated sulphur, two drachms to the ounce, to be applied to the right half of the body; to the left half, an alcoholic solution of coal-tar, diluted one by four or eight parts of water. Internally, a mixture containing sulphate of magnesium, three ounces; bitartrate of potassium, six drachms; precipitated sulphur, one drachm; glycerine, four fluid drachms; peppermint water, four fluid ounces. Dose, a half fluid ounce with a gobletful of water before breakfast. Also a preparation of iron, bark, and arsenic (one-minim dose), to be taken thrice daily. At night a mixture of chloral and bromide of potassium. Both local remedies acted happily, and for five days no preference for one or the other was expressed by the patient. A few days later more improvement was observed upon the side where the tarry solution had been used, and this was then applied, full strength, to the whole surface. Both remedies also had immediate and positive effect in relieving the distressing itching. The skin began to improve and the eruption to decrease within several days after the treatment was insti-

tuted, and at the end of a fortnight very decided benefit was noticeable in the condition of both the general health and the skin. She was well enough a month later to return home, since which time I have heard nothing from her.

The history of the case, extending over three years, shows well the protean character and the multiformity of the disease. It shows the simultaneous occurrence at several periods in the course of the process of erythematous patches, maculo-papules, papular infiltrations, vesico-papules, vesicles, blebs, and pustules. At other periods vesicles and blebs prevailed; sometimes vesicles and pustules; and occasionally vesicles, blebs, and pustules. The lesions were always accompanied by severe itching and more or less burning. Constitutional symptoms at times were marked, consisting of rigors, sensations of alternate heat and cold, and febrile and nervous symptoms. The latter were especially prominent.

The disease of the skin was unquestionably due partly to the depraved condition of general health preceding pregnancy, but more particularly to this latter state itself. It will be remembered that the cutaneous manifestations appeared in the third month of gestation. It was without doubt subsequently kept up by the disordered condition of the menstrual function and the accompanying disturbed nervous system.

At present I shall not consider the disease further than to say that the case may be regarded as representing the multiform variety of dermatitis herpetiformis. Noted at one period, it would have illustrated the vesicular or the papular variety; at another time, the bullous variety; again, the erythematous; while more often, however, the condition was one of multiformity of lesion, including at times the abundant development of peculiar pustules. The latter phase is that which was first described by Hebra as "impetigo herpetiformis." The vesicular variety has figured conspicuously of late years under the head of "herpes gestationis." In a paper recently read before the American Medical Association I have described dermatitis herpetiformis at length, giving its characteristic features, together with its more prominent varieties or phases. I think both the impetigo

herpetiformis of Hebra, and the herpes gestationis of authors, should be placed under dermatitis herpetiformis, both being mere varieties of one pathological process.

The case just considered shows the disease in a severe form, characterised by marked constitutional symptoms; profuse eruption, multiform in character, and appearing in crops; extensive secondary changes in the skin; and itching and burning of the most distressing kind. The patient suffered greatly, the disease for a long period being most rebellious to treatment. Concerning the diagnosis, I may add that as the eruption was noted as one or another set of lesions was out, the disease might easily have been confounded with eczema, herpes, or pemphigus; but keeping the history in mind, and observing the course of the process for some time, the individuality of the disease always asserted itself. It is a distinct and clearly defined disease, which, when once recognised, cannot be confounded with any of the well-known skin diseases.

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## CASE OF DERMATITIS HERPETIFORMIS,

*Illustrating in particular the Pustular Variety (Impetigo Herpetiformis of Hebra).*[1]

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THE following case of this rare disease was brought to my notice by Dr. J. H. Stubbs, of London Grove, Pa., September 28th, 1878. The patient was suffering grievously, and was admitted to the hospital of the University of Pennsylvania. The notes were taken at the date of her admission.

Annie McC—, American by birth, a brunette, æt. 27, single, a domestic, living in London Grove, Chester Co., Pa. There is no family history bearing on the case. She is strong and

[1] Reprinted from the 'Journal of Cutaneous and Venereal Diseases,' vol. ii, No. 8, August, 1884

robust, and has always enjoyed good general health. The disease of the skin from which she is now suffering first made its appearance two years ago, previous to which time she had never experienced any cutaneous disease. It began suddenly on the flexor surfaces of the forearms in the form of a violent attack of itching unaccompanied by eruption. The following day "small water-blisters," the size of pin-heads, appeared in clusters on either elbow. They were very itchy, and were soon ruptured by scratching. In the course of a few days they made their appearance upon the hips, thighs, and knees, while new ones continued to appear about the elbows. Within three or four weeks the other regions of the body, especially the neck, shoulders, back, and buttocks, were invaded. The scalp, ears, chest, mammæ, hands, and feet remained free. The lesions she describes as having been small, variously sized *vesicles*, or "small water-blisters, containing a clear watery fluid." They varied in size from a pin-head to a split pea, the majority being the size of pin-heads. They were irregular in outline, some being rounded, others quite angular, and were considerably raised above the level of the surrounding skin. They manifested no disposition to rupture spontaneously, but were in every instance scratched open, for they itched intensely. As stated, they were in clusters or groups, from three or four to a dozen or more lesions occurring together upon an area the size of a silver dollar. The grouping was irregular, the lesions showing no disposition to form into circles or other peculiar configuration; four or five would frequently be found clustered together.

The eruption continued in this form for a year, manifesting itself from time to time in distinct outbreaks, or crops of lesions, which would appear gradually or suddenly at variable intervals. At times the disease would disappear, when in the course of a week or two a new outbreak would occur, lasting days or weeks, to be again followed by another slight or severe attack, and thus the skin remained in an almost constant state of eruption. At no time was it entirely free of disease for longer than a fortnight.

About a year ago an outbreak manifested itself in which the lesions assumed a distinctly *pustular* character; the attack

was of short duration, lasting only a week or ten days, and the next outbreak was *vesicular and bullous*. Within the past year the lesions have not been so numerous, but they have been larger, and the distress accompanying them greater. Not until within the present month has the disease again assumed the pustular phase. In place of the vesicular and bullous lesions which have existed almost constantly for nearly two years, distinct pustules have appeared, which will be presently considered.

The seasons have in no way influenced the disease, the eruption being quite as annoying in summer as in winter. The itching has been constant and very distressing, and at times has been almost unbearable. She states that it is impossible to describe the intensity and violence of this symptom; that were she debarred from scratching it would be altogether unendurable, for until the vesicular and bullous lesions are ruptured she cannot refrain from scratching; after they are broken down a certain amount of relief is experienced, which lasts until a fresh outbreak threatens. The recent pustules, she states, are much less itchy than the usual vesicular form of eruption.

*Present condition.*—The patient is suffering with a general copious eruption, occupying the greater portion of the trunk and extremities. It manifested itself, it will be remembered, about three weeks ago, and was at its height four or five days since. It consists of numerous, variously sized, rounded or irregularly shaped pustules in all stages of evolution. They are typical pustules, the smallest of them exhibiting a distinctly pustular state. They vary in size from a pin-head to a large pea, the greater number being of the size of small peas; when two or more have coalesced, however, a small or large finger-nail sized lesion exists. In shape, when small, they incline to be acuminated, but as they increase in size they become decidedly flat, with an irregularly rounded or angular outline. They incline to crust in the centre, and to spread in a creeping manner on the periphery, a ring of small flat pustules, isolated or confluent, being frequently present; and where two or more are in close proximity thus almost invariably run together, forming flat broad lesions as large as a quarter-dollar, and sometimes even larger, the

crusting being more or less complete. A bright or deep red areola of considerable size surrounds all of the lesions. In colour the pustules are whitish and opaque, and contain a thin, puriform, pale yellowish or whitish fluid. The walls of the young lesions are distended, but those of the older ones are more or less flaccid, and in many instances are ruptured, the fluid oozing forth, and drying into flat, uneven crusts of a greenish or brownish colour. Here and there are patches of disease, made up not only of confluent lesions, but of two or more distinct groups of lesions. These areas of disease, several inches in diameter, are striking upon the arms and upon the thighs.

The distribution of the lesions is, for the most part, in the form of more or less distinct groups, but there are also disseminated lesions. The groups are irregularly formed, and are, as a rule, composed of from two to four pustules. Clusters of two and three lesions situated in close proximity, within an area of an inch in diameter, are not uncommon, while in some places as many as a half-dozen or more of various sizes may be found. On the anterior aspect of the middle of the thigh is a conspicuous group, composed of a central, unbroken, tensely distended, somewhat acuminated, pea-sized, irregularly shaped pustule, with a vivid, deep red, "puckered" areola, around which are three similar but smaller lesions, the whole occupying an area the size of a quarter-dollar. The grouping, however, viewing it as a feature of the disease, is much less marked than in herpes zoster. In addition to the pustules there are numerous excoriations, blood-crusts, scratch-marks, deeply stained spots, with or without old crusts, and general pigmentation of a dirty yellowish-brownish hue. The disease is the impetigo herpetiformis of Hebra.

October 12th.—The patient stated, upon her admission to the hospital, that the disease had, she thought, passed the height of the attack, and would soon begin to subside; and so the events have proved, but there have been, notwithstanding, sufficient typical new lesions for purposes of study.

They have appeared as distinct pustules, usually the size of pin-heads, preceded by and accompanied with violent itching. Their areolæ at first are insignificant, but in the

course of from twelve to forty-eight hours both areolæ and pustules assume considerable size, the latter flattening out and crusting in the centre, with a somewhat depressed, greenish-yellow, uneven crust. As the crust grows, new, small, flat, frequently indistinctly defined, whitish pustules, pin-head in size, appear in the form of an irregular broken ring just beyond the line of the crust. In the case of large lesions this process is observed to repeat itself several times, or, indeed, until the pustule ceases growing. This concentric arrangement of the lesions, while not conspicuous—not as much so, for example, as in herpes iris—is readily noticeable, and is more marked in some lesions than in others.

The itching has been exceedingly violent, and has been only partially controlled by antipruritic lotions. The patient has scratched incessantly by day and night, without which, she adds, the disease could not be tolerated.

November 1st.—At the present date the attack has almost subsided, and the patient feels that in all probability she will be comparatively well for a brief period until the next outbreak, which she confidently looks for, and which, according to her experience, may announce itself within a week, or perhaps not for a month.

The treatment has been directed with the view of bettering her general condition, although, as has been stated, no marked impairment of general health seems to exist. Saline laxatives, bromide of potassium, and chloral were ordered; locally, lotions of carbolic acid and tar in various combinations were relied upon. While a certain amount of relief was obtained from the lotions, the itching still persisted, and recurred from time to time with all its former violence. No benefit worthy of mention was obtained from the internal remedies.

January 22nd, 1879.—The patient left the hospital shortly after the last note, and for the past three months has been taking a course of arsenic. Dr. Stubbs writes that the character of the eruption has changed since I last saw her, having been lately *papular* and *vesico-papular*, with violent itching. A fortnight ago, while undressing one evening, she was seized with severe itching, and in the course of a alf-hour was well covered with an eruption similar to that

which she now shows. It occupies the entire general surface, and consists of flat, irregularly shaped and sized, indistinctly defined herpetic *papules* and *papulo-vesicles*, seated upon considerably infiltrated reddened skin, which is everywhere so excoriated that it is difficult to find lesions that have not been scratched. Excoriations and blood-crusts are conspicuous. Here and there upon the trunk and extremities, especially upon the back, arms, buttocks, and thighs, there are distinct patches of pin-head sized, mostly flat *vesicles*. They are small and are ill defined, so much so that at a distance they would scarcely be detected. Some of the patches contain as many as a dozen or more, other groups not more than three or four. Smaller and disseminated lesions of the same kind exist on the forehead and neck. There are no pustules; none have formed since last October. She states that the eruption comes out and disappears every few days, the itching being most severe in the interim. She is kept awake the greater part of the night, and is exhausted from the long-continued itching.

May 16th.—She recovered from the attack in January, in February, and remained comparatively well about ten days, when a new outbreak was announced, which appeared very gradually in the same form as before, namely, as small, flat, grouped, abortive *papules* and *vesico-papules*. She has suffered two like attacks since, from the last of which she is just recovering.

Under date of August 18th, 1879, Dr. Stubbs writes that the patient is again suffering greatly from an outbreak, and that no relief is afforded by any of the remedies used. He further adds, "I do not know what to call the disease; sometimes it is pustular, at other times it is vesicular or papular, while sometimes wheals and boil-like lesions form. It is now vesicular." Two months later (October 16th, 1879) the doctor writes, "Her condition now is the same as when I first sent her to you one year ago; the lesions are *pustular*. We have not had this condition from that time until now. On the 5th of this month three pustules came on her knees; others rapidly followed on other parts. She can get scarcely any sleep. She has had no appetite for two or three weeks." I subsequently saw the patient again during an

attack, her condition being about the same as the last note.

Early in 1883 (January 17th) I received a communication from Dr. Stubbs stating that the patient was still afflicted, although she now suffered less severely than formerly. "She has since been married, and has had one child. *During pregnancy the disease of the skin gave her no trouble, and most of that period she was quite clear.*[1] Last summer the mucous membrane of the mouth, throat, and eyes became inflamed, dry, and hot, and finally an eruption, which was the same as that on the skin, appeared. The labia and vagina have never been affected. She has not been under treatment of late for the cutaneous disease. The eruption, as before, is still confined chiefly to the back and flexor surfaces of the extremities."

I would add that no treatment used in this case seemed to exert any beneficial effect, the internal remedies prescribed including arsenic in small and large doses, quinia, iron, sulphur, saline laxatives, and alkalies. Externally, weak and strong ointments and lotions of carbolic acid, tar, and mercurials were all tried on different occasions, affording only temporary relief. The case illustrates several varieties of the disease, but more particularly the pustular (the "impetigo herpetiformis" of Hebra), which condition existed when she first came under my observation. For an account of dermatitis herpetiformis I must refer to abstracts[2] of my communication recently presented to the American Medical Association.

[1] The italics are mine.

[2] 'Philad. Med. Times,' May 17th, 1884, p. 603, and 'New York Med. Journ.,' May 17th, 1884, p. 562.

# DERMATITIS HERPETIFORMIS:

## ITS RELATION TO SO-CALLED IMPETIGO HERPETIFORMIS.[1]

In a recent communication made before the American Medical Association I described a remarkable disease of the skin under the name dermatitis herpetiformis. The observations there recorded are the result of many years' study upon this subject, several of the cases from which my data were derived having been under surveillance for a number of years; and it is this fact, in my opinion, which makes the notes especially valuable. Had the notes of any one of these cases been confined to the condition as shown by a single attack, we certainly should have had a very different idea of the process as a whole from that which is now held. In the study of diseases of the skin the natural course of the process must not be lost sight of. We cannot make the diagnosis in all cases from the presence of the lesion alone; we must note further its evolution and general characteristics. This remark is especially applicable to multiform or protean diseases—such, for example, as the affection under consideration.

Permit me first to state briefly what dermatitis herpetiformis stands for, according to my definition. It is a well-defined disease, characterised by a variety of symptoms, which, although they appear dissimilar, and perhaps in no way related at first sight, will sooner or later be found to be but different expressions of one process. It is one of the

[1] Read before the American Dermatological Association, at its eighth annual meeting, August 27th, 1884. Reprinted from the 'American Journal of the Medical Sciences,' October, 1884.

rarer cutaneous manifestations, only one variety of which has been heretofore carefully described, namely, the pustular, by Hebra, under the name of impetigo herpetiformis.

The disease in severe cases is ushered in with more or less constitutional and febrile disturbance, characterised by malaise, shiverings, alternate hot and cold sensations, or fever. Itching or burning is early announced, followed in the course of from twelve to forty-eight hours by more or less eruption, consisting of erythematous, maculo-papular, papular, tubercular, vesico-papular, vesicular, vesico-bullous, bullous, or pustular lesions—as a rule all having peculiarities which distinguish them from the manifestations characterising other well-known diseases.

The erythematous lesions are usually in the form of patches of an erythema multiforme-like or urticarial kind, varying in size from a small coin to the palm of the hand, and of an irregularly rounded shape, tending, when in proximity, to coalesce. Some are ill-defined; others have a sharp, somewhat marginate outline. They are usually more or less raised, somewhat less in the cases I have met with than in either erythema multiforme or urticaria. They resemble especially the lesions of the former of these diseases. They are not so fugitive as in urticaria. I may even say that they bear more resemblance to ill-defined patches of erythema multiforme than to any other disease. These remarks may be taken to apply in part also to the maculo-papular lesions, but the papules and tubercles are different, being imperfectly defined inflammatory elevations, variable in size, shape, and consistence. The vesico-papules are similar to those encountered in erythema multiforme or in the early stages of herpes iris, and where numerous and close together, occurring upon thickened pigmented skin, may resemble the first stages of confluent variola.

The vesicular lesions vary in size from a pin-head to a pea; are flat or slightly raised, broad, angular or irregular in outline; of a pale yellow, straw-coloured hue, tensely distended; glistening, and without areolæ unless closely grouped. The blebs vary in size from a pea to a pigeon's egg or even a hen's egg, and possess most of the features enumerated in speaking of the vesicles. They are, however,

raised, as in the case of most other blebs, as of pemphigus, and may have opalescent, cloudy, hæmorrhagic, or even pustular contents, although the pustules to be presently described do not pass through stages of evolution from the bleb, but begin usually as clearly defined small pustules.

The pustules are peculiar. They begin as small, flat, pin-head sized, whitish lesions, which grow, as a rule, to the size of a small pea, when they are surrounded by a deep red, "angry-looking," more or less raised areola. Their course up to this point occupies from two to six days. Sometimes two or three small pustules appear as a little cluster; as they grow they run together, forming a large pustule. About the time the lesion is at its height, one, two, four, or more new, small, flat pustular points or distinct pustules begin to appear in the form of a ring, or as a segment of a circle, immediately around the original lesion, which by this time is somewhat crusted. As these increase in size they are absorbed into the first pustules, the whole being covered with a yellowish, greenish, or brownish, flat, adherent crust. New small pustules may still continue to form around this lesion as before, or the process may be arrested. The number of pustules varies; there may be half a dozen scattered about, or hundreds, some the size of a pin-head or of a pea, others as large as a quarter-dollar. When they are in close proximity and have run together, large patches may form.

I may now direct attention to a peculiarity of the several lesions of the disease, and this is the tendency for two or more kinds to exist simultaneously—as, for example, vesicles, vesico-blebs, and blebs; or it may be vesicles, blebs, and pustules—both rare combinations in the list of cutaneous diseases. The order of manifestation is variable. There is no definite order in the evolution of the lesions during an attack, nor even in relapses or in recurrences of the disease. This irregularity in the evolution of the process is peculiar, and must be regarded as one of the marked features of the disease. It has been present in almost all of the cases that have been under my observation. The longer the patient has been under observation the more frequently has this feature asserted itself. An attack beginning as an erythema

may pass rapidly into the vesicular or bullous variety, to be in a few weeks succeeded by the pustular variety, this again by the vesicular or bullous variety, followed by perhaps the pustular for the second time, these several changes or varieties of the disease appearing, it may be, in the course of a month or a year. The mixture or commingling of the several lesions, two or more kinds often showing themselves during an attack of any one variety, certain lesions decidedly predominating and giving the type to the eruption, is striking. Thus in the pustular variety it is not uncommon to note vesicles, vesico-blebs, and blebs seated in close proximity to the pustules; and in the bullous variety to observe pustules almost contiguous to the blebs.

Multiformity, therefore, is the rule; and where cases remain under notice for a period of years, and repeated recurrences are recorded, this feature is in almost all instances one which impresses itself alike on patient and physician. Eczema, as we all well know, is often multiform, but surely this disease far exceeds eczema in the extent to which this character may go. It is not only multiform, but is capriciously so, the various manifestations often taking place in rapid succession, but especially in the case of new crops of lesions and relapses. At one period it is strictly vesicular, this variety continuing it may be several weeks or months, several attacks of the same kind appearing during this time; on another occasion it will be vesicular and bullous, or alternately vesicular and pustular. The tendency is to be vesicular and bullous, the erythematous and pustular manifestations being rarer.

The general character of the eruption is herpetic, in the sense that the lesions incline to group or to appear in small or large patches, and further that where they form in proximity they tend to coalesce. This feature, however, is variable. The arrangement may be in little groups of two or three or four lesions, or, as in the case of the pustules, they may form in circles or segments of circles around the original lesion. In both the erythematous and pustular varieties there is a marked disposition to spread on the periphery, and in the former variety a disposition to creep, causing at times marginate patches. In the vesicular and

bullous varieties there is less tendency to group, and the vesicles and blebs may even be disseminated. In the same patient with different attacks I have noted the lesions disseminated and grouped. It frequently happens when the eruption is abundant that grouping will occur here and there, while in between the groups and elsewhere the vesicles and blebs will be disseminated. Another evidence of the herpetic nature of the disease is noted in the irregularity of the lesions, especially in the case of the papules, vesicles, blebs, and pustules. The irregular, angular, or stellate outlines of vesicles and blebs, as a rule without marked areolæ, are strongly suggestive of the nature of the process. Pigmentation must also be mentioned as a symptom common to all varieties, and in chronic cases is usually pronounced. Considerable thickening of the skin is also marked in such cases. In almost all instances, at all periods of the eruption, an irritable state of the skin, comprising itching, pricking sensations, heat and burning, is a prominent symptom. In most cases it precedes the outbreak for several days, becoming more pronounced as the eruption reaches its height, then declining and again asserting itself with a new crop of lesions. Itching is the sensation generally complained of. It is usually severe, causing great distress of mind and body. In most of the cases that I have encountered it has shown itself intense, and to be far more formidable than in an eczema of like grade. Burning sensations also are frequently described, especially in connection with the pustular variety ; and when the varieties have changed from one to another, as the vesicular to the pustular and back again, itching and burning will exist alternately or be present together, constituting a sensation said to be much the most trying to bear. Sometimes it happens that an attack of the pustular manifestation, especially when the lesions remain small, is unaccompanied by subjective symptoms. I recall one such case in a man where the pustules were abundant, the patient stating that at the time he suffered but little inconvenience from the eruption ; but in a subsequent attack, of the vesicular and pustular varieties combined, he was greatly distressed with itching and burning.

The disease usually runs a chronic course, extending over years, repeated attacks appearing from time to time at intervals of months or years. I have known cases where it has continued, most rebellious to treatment, for five, ten, and fifteen years. During these long periods the patient has suffered more or less continuously, sometimes with periods of months of comparative or entire freedom from the disease; but the tendency is to persist, frequently in a milder form as time rolls on. In some cases I believe complete recovery has taken place, but with the histories at hand I cannot speak positively on this point. In chronic cases the process often takes on a subacute form. The disease attacks both sexes, and usually in early or middle adult life. It occurs in single as well as in married women, though more frequently in the latter, especially during pregnancy and in the parturient state. For its cause we must look to the nervous system. It is without question a neurotic disease, in some cases being manifestly under the control of the nervous system. This statement need excite no surprise when we consider the large number of similar cutaneous diseases traceable directly to impaired nerve-force, a list which is yearly being enlarged.

With these introductory remarks upon the disease I shall proceed to consider the subject of its relation to the impetigo herpetiformis of Hebra. I have already (in a paper read before the American Medical Association at its last meeting[1]) expressed the opinion that the form of disease described by Hebra was the same as the pustular variety of dermatitis herpetiformis, and that it constituted merely one variety of an extensive multiform disease, and that therefore the term "impetigo" was inappropriate. I also made the statement that the so-called impetigo herpetiformis, in opposition to the views of Hebra, Kaposi, Neumann, and other dermatologists, occurred in men as well as in women, and in women independent of pregnancy.

If we look into the history of impetigo herpetiformis we shall find that the name dates back to 1872, when Hebra first described the disease in a paper entitled "On some

[1] May 6th, 1884. For abstract see 'Philad. Med. Times,' May 17th, 1884, p. 603, and 'New York Med. Journ.,' May 17th, 1884, p. 562.

Affections of the Skin occurring in Pregnant and Puerperal Women,"[1] his remarks being based upon five cases observed by him. Before this, however, Bärensprung had met with a striking case of the disease. In the 'Atlas of Skin Diseases,' by Hebra and Bärensprung,[2] this latter author figures a case with the title "herpes circinatus," which portrays a peculiar and striking form of circinate and annular pustular disease, which Hebra subsequently stated was an example of his impetigo herpetiformis. No notes of the case accompanied the portrait, nor is any information given concerning the disease beyond the statement that it illustrates a rare form of herpes circinatus. It manifestly portrays the affection under discussion.

Two years later Auspitz,[3] with the name "herpes vegetans," reported two cases which I think without doubt represent unusual forms of the disease we are considering. The first case (which was under the care of a "Dr. G." at the time of the outbreak, and who gave Dr. Auspitz an account of the eruption) was a pregnant woman. The cutaneous disease began as a bright red erythema upon the abdomen, which soon passed into a moist, itching, and burning surface, studded here and there with vesicles. The disease at the time was regarded as an eczema. The vesicles, in groups, continued to appear, passing into pustules closely crowded and covered with crusts, the condition resembling a papillomatous vegetation ("*fleischwärzenartigen Wucherung*"). Febrile disturbance existed, and the patient suddenly collapsed with œdema of the lungs. There was no autopsy.

The second case is one which was under Hebra's care in the hospital, and was one of the five cases of Hebra. The woman was twenty-six years old, married, and in the sixth month of pregnancy. The eruption consisted of reddened skin with vesicles and pustules, varying in size from a pea to a bean, disseminated and grouped in a circular form. In the inguinal region there were dollar-sized, red, excoriated, moist patches covered with greenish crusts, with here and

[1] 'Wiener med. Wochensch.,' No. 48, 1872.

[2] Tafel viii, Erlangen, 1867.

[3] 'Archiv für Derm. u. Syph.,' 1869, p. 247.

there vesicles and pustules. On the lower extremities there were disseminated pustules and vesicles. There was burning and itching, also marked febrile disturbance. Later some of the patches assumed a papillomatous or vegetating appearance, "like acuminated warts." The eruption increased in extent and intensity, the lesions spreading on the periphery of the patches, the patient being very ill. She was delivered of a dead child, but a week later died with symptoms of diarrhœa and delirium. The autopsy showed "endometritis, oöphoritis, metrosalpingitis, and peritonitis." Dr. Auspitz sums up the characters of the disease as follows:—1. The occurrence of grouped vesicles and pustules with eczematous infiltration between the lesions. 2. Cutaneous vegetation on these patches of condyloma-like tumours. 3. The development of the disease in both cases in pregnant women. The reporter regarded the disease as new, and thought that the term "herpes vegetans" expressed the condition in both cases.

We may now consider Hebra's paper. In the article above alluded to, this distinguished observer[1] called attention to an eruption of which at the time he had encountered only five examples, all occurring in pregnant and puerperal women. It was characterised by pustules filled with pus at their first appearance, and by these affecting a peculiar mode of grouping and peripheric extension. In almost every case they first appeared at the inner surface of the thighs, partly in groups the size of a dime, and partly as separate pustules the size of a pin-head. Successive crops immediately followed, extending towards the periphery in a circular or iris form, so that in the course of a few days a gradual invasion took place on the thighs, abdomen, legs, arms, hands, and feet, and afterwards on the neck, face, and scalp. While at the centre of each group the pustules became covered with flat brownish scabs, at the circumference new ones filled with yellow pus were being constantly produced. In this disposition they resembled "herpes iris circinatus;" but as from the very first, Hebra states, it was a pustular disease, it must be regarded as a form of impetigo, and

[1] 'Amer. Journ. of Syph. and Derm.,' April, 1873, p. 156, translated from 'Wiener med. Wochensch.,' No. 48, 1872.

might, from its circular mode of grouping, be termed "impetigo herpetiformis."

The affection throughout its whole course was attended by intense fever, a dry tongue, and great prostration. In three of these cases this reproduction of the pustules continued with more or less rapidity until the patient died; while in the other two, after several weeks' duration, the pustules dried up, the thick scabs finally falling off and leaving the skin beneath healthy but strongly pigmented. Some of the pustules, instead of drying, especially at the bends of the joints, were converted into a greyish, stinking mass, which, lying on a red and moistened base, assumed an eczematous appearance. Only one out of the five cases finally survived.[1] Each outbreak of pustules was preceded by shivering, which was followed by febrile action that lasted some days. Of the five women, three had been delivered from two to five weeks before admission, and two came in during the last month of pregnancy. The appearances were the same both before and after delivery. The autopsies of the four women who died revealed no certain cause of death. Neither the mode of life, employment, nor constitution of these patients threw any light upon the origin of this affection. In none of them was there any symptom of syphilis. In the absence of all other etiological data, and seeing that these cases all occurred in pregnant women, it might be stated, in connection with the cases already referred to in this paper, as most probable that these instances of herpetiform impetigo were dependent upon a diseased change in the genital apparatus. Several years later (1876) Hebra again takes up the subject in his 'Atlas of Skin Diseases,'[2] and gives two portraits. He says, in allusion to the inappropriateness of regarding it as a form of herpes, "The disease under consideration does not appear in the form of vesicles and circles of vesicles, nor does it run an acute or typical course. . . . It makes its appearance in the form of pustules, resembling in the manner of spreading herpes iris and circinatus, and on this account the disease had better be termed impetigo herpetiformis."

[1] In Hans Hebra's work on 'Diseases of the Skin,' Braunschweig, 1884, p. 198, it is stated that this patient also died subsequently during a relapse.

[2] Heft 9, Tafeln ix and x, text, p. 111.

The disease, in the first article, is graphically but very briefly described. The leading features only are touched upon. There are many points of interest which barely receive mention—such, for example, as the description of the lesions, their multiformity, and their evolution. These features, however, are brought out in the report of a case by Auspitz, already referred to, and also in the case reported by Geber, to be spoken of presently. This criticism is made for the reason that, I think, had Hebra's account of the disease been more complete, the affection would have received more attention at the hands of dermatologists. The description was scarcely full enough to enable observers to recognise the affection. The subject, I am sure, has been received by many with doubt as to the precise features characterising the disease. It may be added that all of Hebra's cases were severe, and that the two portraits given in his 'Atlas of Skin Diseases' show the disease at its height, and are sketched with a bold brush and in strong colours.

One of Hebra's cases, as stated, was reported in full by Geber.[1] The patient was a woman, a dark blonde, æt. 25, in the ninth month of pregnancy. The skin disease had existed four weeks. In consisted of numerous disseminated, miliary, and hempseed-sized vesicles. Here and there they occurred in groups of two, three, or more, in which event they ran together, crusted, and spread on the periphery, in the form of rings of pustules. In this manner, as in herpes iris, patches as large as a dollar or even the palm of the hand were formed, the centres being crusted with greenish-yellow crusts. The largest patches existed on the breasts, on the flexor surfaces of the thighs, on the abdomen, and about the flexures of the knees and elbows. The tongue also showed symptoms of the disease. After delivery the lesions began to desiccate, and abundant desquamation set in, which, however, was shortly afterwards followed by signs of moist eczema about the neck and under the breasts. Three days after delivery diarrhœa occurred; the temperature and pulse both rose, and there were rigors. Later, the skin

[1] 'Bericht aus dem Wiener allg. Krankenhause für 1871,' von Hebra's Klinik, Wien, 1872; abstract in 'Archiv für Derm. u. Syph.,' Heft 1, 1873, p. 169.

became clear of eruption, and the general symptoms ceased. Two weeks afterwards a relapse of the cutaneous lesions took place in the form of groups of vesicles involving the whole surface, pursuing the same course as before. A month later the patient was dismissed from the hospital. The description of the lesions in this case corresponds with the condition as portrayed in one of the plates in Hebra's Atlas, and it is probable that this case was utilised for the portrait.

Neumann first described the impetigo herpetiformis of Hebra in the third edition of his 'Handbook of Skin Diseases,'[1] in considering herpes zoster. A brief account of the disease, together with Auspitz's case, is given, and the titles "herpes pyæmicus" and "herpes puerperalis" suggested. In the fourth and fifth editions it finds a place under impetigo herpetiformis, a very brief account only being given, accompanied in the last edition with a woodcut illustrating the anatomy of the lesion. In speaking of herpes this author, in the third edition of his 'Handbook of Skin Diseases,'[2] describes at length an affection which he regarded as a form of herpes, a view which, as we shall see, he subsequently retracted. The subject was later made the occasion of a paper bearing the title "Dermatitis Circumscripta Herpetiformis,"[3] under which name the disease appears in the fourth edition of his 'Handbook' (p. 347). He regarded the disease as "herpes chronicus," and so named it. Shortly after this publication, Hebra, in the second edition of his great work on diseases of the skin (p. 311), expressed himself to the effect that this affection was probably not herpes, but rather lichen ruber occurring in groups. Neumann again described the disease in the fourth edition of his 'Handbook' with the same name (dermatitis circumscripta herpetiformis), giving special attention to the pathological anatomy. In the fifth edition of his work, however (p. 310), we find dermatitis circumscripta herpetiformis synonymous with lichen planus, being regarded as distinct from lichen ruber. I have felt it incumbent upon

[1] Wien, 1873, p. 185.
[2] 'Viertelj. für Derm. u. Syph.,' 1875, Heft 1, p. 41.
[3] Wien, 1873, p. 188.

me, in connection with my subject, to give this history of the dermatitis circumscripta herpetiformis of Neumann, lest it should be thought by some to be the same as my dermatitis herpetiformis.

I may now refer to Heitzmann's interesting case. This author, in a paper[1] read before the American Dermatological Association, reports a case of impetigo herpetiformis under the heading "On the Relation of Impetigo Herpetiformis to Pemphigus." The patient was a well-nourished woman, æt. 52, who had given birth to several healthy children. She had had eczema the previous year, which had been cured. The mucous membrane of the lower lip, the gum, the cheeks, and the tongue, on the lateral parts, were the seat of flat blebs, partly confluent and partly coated with a greyish-yellow epithelial layer, which on many places being torn away left an intensely red, excoriated, bleeding surface. The right auricle was the seat of an eruption, also the skin of the neck, and the folds below the mammæ, the surface being dark red, infiltrated, and thickened, as if the seat of eczema rubrum. On many places the periphery showed groups of small pustules. There was no fever; menstruation had ceased naturally several years before; nor was there any uterine disease. New eruptions of blebs occurred every few days on the mucous membrane of the oral cavity, preceded by sharp pains and a severe rigor. Pustules also appeared on the mucous membrane of the nose, accompanied by high fever, followed by erysipelas of the face. They, moreover, appeared on the body, on the genitals, and about the umbilicus, the sites of former lesions being reddish brown, pigmented, or pale greyish blue, coated with a thick, exuberant, irregular epidermal layer. Several weeks afterwards, during which period she had partly recovered, a few flaccid blebs appeared. Two weeks later, within two or three days, there appeared a great many "pemphigus blebs" on the abdomen, the back, and the feet, accompanied with high fever, weak pulse, signs of collapse, brain symptoms, and manifold other serious constitutional disturbances. The mouth and cutaneous manifestations were on several occasions repeated during the next three months,

[1] 'Archives of Dermatology,' Jan., 1878.

followed by emaciation, œdema, bedsores, ascites, the patient dying from œdema of the brain. Heitzmann concludes his remarks by stating that the disease is closely allied to pemphigus, and the diseases must be regarded as being kindred to each other.

In recent English and American literature, with a few exceptions, no reference is made to impetigo herpetiformis, either as a distinctive disease or to the cases described by Hebra. Thus the books of Liveing,[1] Morris,[2] Bulkley,[3] and Fox[4] contain no allusion to the subject. Hyde,[5] in his 'Treatise on Diseases of the Skin,' defines impetigo herpetiformis to be "a cutaneous disease of women, frequently complicating the puerperal state, characterised by the occurrence upon the skin and mucous membranes of concentrically grouped pustules, and by a febrile condition which usually terminates fatally." A description is given of the affection, mainly based upon the cases of Hebra, with an allusion to Duhring's observations.

Besnier and Doyon, eminent French dermatologists, and the translators of Kaposi's 'Pathologie und Therapie der Hautkrankheiten' (Paris, 1881, vol. ii, p. 49), in a note state that the author's description of imepetigo herpetiformis is not sufficiently extended to base an opinion upon, and that it is necessary first to bring forward a record of the facts. They object to the denomination impetigo herpetiformis, first, because "la dermatite pustuleuse circinée et excentrique," of which they state the affection in question is an example, cannot be grouped with impetigo as this term is used by French dermatologists; secondly, because the title herpetiform can be applied only to an affection truly of the form of herpes, that is to say, resembling the herpes type (herpes labialis, herpes zoster, &c.), and not to a special eruption which does not belong exclusively to herpes. They regard the disease as of septicæmic origin.

[1] 'Handbook of the Diagnosis of Skin Diseases,' Amer. ed., New York, 1879.

[2] 'Skin Diseases,' London, 1879.

[3] 'Manual of Skin Diseases,' New York, 1882.

[4] 'Epitome of Skin Diseases,' third Amer. ed., revised by T. C. Fox, Philad., 1883.

[5] Philadelphia, 1883.

me, in connection with m[illegible] disease is rare in France, the dermatitis circumscri[illegible] French accoucheurs, who it should be thought by s[illegible] r. Behrend, in his 'Lehr. titis herpetiformis. [illegible] escribes the disease briefly,

I may now refer to H[illegible] servations for the account, author, in a paper[1] read b[illegible] Association, reports a ca[illegible] n his work,[3] in considering the heading "On the Rel[illegible] that eleven cases have been Pemphigus." The pati[illegible] Vienna General Hospital, all æt. 52, who had given [illegible] for the most part in the She had had eczema t[illegible] n of the eleven cases ended cured. The mucous me[illegible] e case. In one apparent the cheeks, and the ton[illegible] fever. In a few weeks was seat of flat blebs, partly [illegible] In another the disease, greyish-yellow epitheli[illegible] succeeding pregnancies followed torn away left an inten[illegible] third pregnancy. In Hans The right auricle was [illegible] of impetigo herpetiformis of the neck, and the [illegible] but nothing new is added being dark red, infilt[illegible] of the disease. He states eczema rubrum. O[illegible] Vienna about ten cases of the groups of small pustu[illegible] women towards the end of tion had ceased na[illegible] there any uterine di[illegible] there exists no room for every few days on [illegible] impetigo herpetiformis preceded by sharp p[illegible] dermatitis herpetiformis. appeared on the m[illegible] dental, as must be seen, by high fever, foll[illegible] and if this be the moreover, appeared [illegible] must include a variety of the umbilicus, th[illegible] these varieties of dermatitis brown, pigmented, [illegible] briefly in the second exuberant, irregul[illegible] In speaking of the wards, during whi[illegible] and also in my paper read flaccid blebs app[illegible] already alluded to. three days, ther[illegible] interesting. Our know. blebs" on the a[illegible] panied with high[illegible] Duhring's Treatise on Skin symptoms, and m[illegible] ances. The mou[illegible] several occasions[illegible] Braunschweig, 1884,

[1] [illegible]

ledge of the disease, if my views be correct, is yet in its infancy. As clinical reports and other information come to light it will be found that it will assume an important position in dermatology. Many cases that have hitherto been regarded as obscure or as difficult of classification will become plain. Cutaneous medicine covers an extended field in pathology, and to include the numerous manifestations now known to exist both terms and definitions must be broad. The tendency in the past has been to study symptoms rather than processes. In the future it is to be hoped we shall be able to bring symptoms together, to reduce rather than to augment the number of diseases, and to classify them according to their pathology.

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## NOTES

OF A

# CASE OF DERMATITIS HERPETIFORMIS

## DURING THIRTEEN YEARS.[1]

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THE notes here presented, portraying the disease I have named dermatitis herpetiformis, are of such interest that they are given in full, with the view of directing attention to the many and peculiar phases this remarkable disease may assume. The long period the disease was under observation, and the extended notes which were made at the time, give us valuable information on the natural course of the disease—a point always of importance in the study of cutaneous affections.

H. H. McK—, æt. 31, an American, and a painter by occupation, was admitted to the Philadelphia Dispensary for

[1] Reprinted from the 'New York Medical Journal' for November 15th, 1884.

Skin Diseases, Philadelphia, July 6th, 1874. He was in impaired health, and had been suffering from the skin disease for which he sought relief since 1871, a period of three years. He was of small frame and spare, and was apparently in a state of nervous exhaustion, being weak, tremulous, dyspeptic, and despondent about his condition. He was married, and was temperate in his habits.

The following clear history was obtained :—In 1871 the first disease of the skin ever experienced manifested itself in the form of lesions which he describes as "hives." They came unexpectedly and suddenly, and occupied every portion of the surface except the face, being particularly numerous and thickly set about the elbows and knees. They were erythematous in character, and were split-pea and finger-nail sized, raised and flat. Some were discrete, but the greater number were confluent. The whole surface was pretty well covered with the efflorescence, and was the seat of violent itching. The attack is described as having possessed all the features of urticaria. It gradually subsided in the course of three or four days, when a crop of small, rounded, flat *pustules* began to appear here and there, especially about the knees and elbows, accompanied by itching. They increased slowly in size, and crusted with a brownish, adherent crust. A number of them came out, varying in size from a split pea to a small finger-nail. They all ran a similar course, lasting from five or six days to a fortnight. By the end of four weeks they had completely disappeared, but, almost before the crusts of the earlier lesions had fallen off, a crop of *vesicles* and *blebs*, of all sizes and shapes, suddenly appeared, distributed quite generally over the extremities and upon the face. There were great numbers of them upon the face, and they varied in size here from a pin-head to a hazel-nut. Upon the general surface they were mostly small—pin-head and split-pea sized. Some were raised and semi-globular in form ; others were flat. The lesions, as stated, were *vesicles* and *blebs* having perfectly clear contents, and were without areolæ. They were very itchy. There were no signs of pustules.

This attack lasted about two months, new vesicles and blebs appearing from day to day, and gradually subsided.

The patient speaks of the experience as having been very trying, not only on account of the presence of the lesions and the discharge and crusting, but also because of the itching.

For several months he remained comparatively well, when a copious mixed eruption—composed of small *vesicles*, *pustules*, *vesico-pustules*, and *vesico-papules*, accompanied with itching—made its appearance upon the regions previously affected. This was the first occasion of the lesions being distinctly multiform. This attack lasted only a fortnight, vanishing quite suddenly, and leaving the skin in a better state than for months. This last form of eruption, however, soon recurred, lasting, as previously, but a few weeks, and, as before, leaving him apparently quite well. He has had many attacks of this character, at intervals of a few months, up to the present time. The disease has thus continued its course, uninfluenced by the varied treatment to which he has been subjected. He does not think that the seasons have at all influenced the natural course of the disease.

It was at this period (July, 1874) that the patient first presented himself to me. He showed the pustular phase of the disease, which had but recently made its appearance. There were about a score of disseminated, split-pea and finger-nail sized, flat, mostly crusted with a yellowish-brown, adherent, flat, ecthyma-form crust, here and there distinctly clustered *pustules*. They occupied the lumbar and sacral regions, the buttocks, and the elbows and knees. They had appeared a fortnight previously, and had been and were still accompanied by itching. The more recent lesions I observed were surrounded with bright red, highly inflammatory areolæ, and were peculiar in that they inclined to crust in their centre and to spread on the periphery, forming more or less distinct, narrow rings of pustulation immediately beyond the line of the crust. This feature was not constant, but existed in connection with a number of the lesions, and constituted a symptom which at once arrested my attention.

The case was regarded as an unusual one, the form of disease being entirely new to me, and this observation was

so recorded in connection with the notes. The lesions b
a close resemblance to cachectic ecthyma, but the localit
attacked were those seldom invaded in this latter disea
The pustular variety of eczema, aggravated by some irritati
application, also suggested itself, as did, moreover, impet
contagiosa. The contents of several of the pustules, as v
as the crusts, were at the same time submitted to mic
scopical examination with a view of determining if
parasite was present. The patient was placed upon a sal
laxative mixture, together with full doses of the tincture
chloride of iron. No local treatment was ordered.
case remained under observation three months, and, acc
ing to the notes recorded, the patient was in about the s
condition at the expiration of this period as upon admissi
the skin, however, underwent several decided changes dur
the three months, having been on one occasion almost w
but the lesions soon reappeared. The disease did not s
to be in the least degree influenced by treatment, whet
internal or local, new pustules, small and large, appear
from week to week. In November, 1874, he ceased atte
ing the dispensary, much discouraged. The diagnosis
as obscure at this time as on admission.

In January, 1879, four years after the foregoing note,
presented himself for treatment at the hospital of the Univ
sity of Pennsylvania. I at once recognised my former pati
of the Dispensary for Skin Diseases. He stated that he
still afflicted, but that until recently it had existed in a mil
form, and that he had experienced intervals of from one
six months of comparative freedom, but he had never b
entirely free of eruption. The general health had fai
considerably, the nervous system had become more disturb
and he was habitually constipated. During the four ye
he had employed various internal and local remedies,
without benefit. The general course of the disease had b
about the same as when under observation four years befo
He had noted four kinds of lesions, which would manif
themselves together or in different attacks of eruptio
These were true *pustules*, containing from the beginnin
whitish puriform fluid, and of variable size, from a pin-h
to a silver quarter-dollar; *vesicles*, containing a clear yell

ish fluid, likewise of variable size; *blebs*, varying in size from a split pea to a half-cherry; and, lastly, *papulo-vesicles*, acuminate in form, and exuding a small amount of a serous, gluey, gummy product. The "watery blisters," as he termed the vesicles and blebs, had, on every occasion of their appearance, been very itchy; the pustules itched but little. The vesicles and blebs grew rapidly, reaching their full size in a few days, and were accompanied by but slight inflammation about their bases; the pustules, on the other hand, were always markedly inflammatory. On each occasion of the pustular form of eruption he "felt badly," and was in poor general health. He had had but three or four "pustular attacks," the rest having all been vesicular and bullous. The disease, whatever the form of lesion, always manifested itself in attacks, which would announce themselves at intervals of weeks or months, one scarcely subsiding before another would appear. He does not remember that any of the attacks were preceded by chills or fever. The seasons seemed to exert no influence on the course of the disease. He noticed that frequently the lesions inclined to come out in the form of groups or clusters, four or five appearing within a radius of an inch or two, and often coalescing. The regions invaded have been the same as in the beginning—the face, neck, elbows, knees, sacral region, and buttocks being the favourite localities. The genitalia, hands, and feet have generally been free; the palms and soles have always escaped.

His condition when I saw him in January, 1879, was very similar to that recorded as existing when I first observed the case in 1874, and therefore need not be described in detail; so much did his condition resemble the former state, as regards the general character and distribution of the eruption, that it seemed as though the very same lesions were present. The pustules were the only lesions. They were of all sizes, most of them being as large as dimes and quarter-dollars; rounded or irregular in shape; crusted with yellowish-brown crusts; flat; here and there clustered, or about coalescing; in all stages of development, and surrounded by highly inflamed, extended, bright red areolæ. They, moreover, possessed the characteristic before noted of ex-

tending around the periphery and just beyond the line of the central crusting. The patient was ordered wine of iron, with three-minim doses of Liquor Potassii Arsenitis thrice daily. With the view of observing the course of the lesions, local treatment was withheld.

March 11th, 1879.—The case has been under constant observation since the previous note, six weeks ago, during which time the disease has behaved much as it did on the first occasion I had of studying it. The lesions have pursued a rather slow course, considering their highly inflammatory nature, an average pustule lasting, from the beginning until the crust dropped off, from two to three weeks. Many new lesions, all strictly pustular in character, have from time to time appeared, as a rule, in crops, while the older ones have, at the end of a variable period, disappeared, leaving persistent dark red, brownish, pigmented marks. No scars remain. One peculiarity of mature pustules has not been referred to, namely, the tendency for the inflamed skin around the crust to pucker, giving the skin a wrinkled, drawn-up, glistening appearance. The disposition of the lesions to group has always been present, though at times only to a slight extent. It has not, however, been observed with all of the lesions, many appearing singly. As they increased in size there would generally be noted a number of discrete or confluent small pin-head sized, flat pustules immediately around the circumference of the original lesion in the form of a ring. This feature varied, being much more pronounced in some cases than in others, and at times was wanting. The pustules, however, seemed to grow in this manner, a new ring of minute pustular points springing up every few days around the crust until the lesion reached its determinate size. The crusts were adherent upon lifting them up, a superficial, reddish excoriation covered with a slight puriform fluid—as in the case of ecthyma—presented itself. Little or no bleeding occurred. Itching has not been severe, but the lesions have "felt sore."

Three nights ago he was attacked with violent itching of the general surface, accompanied with an efflorescence which he describes as having been identical with certain attacks before experienced on several occasions, and which was

plainly urticarial in nature. It began, while in bed, upon the arms, but soon extended itself over the whole surface except the hands and feet, the backs, as well as the palms and soles, remaining free. The eruption was *erythematous* and very red, and exceedingly itchy; so much so that he was kept awake all night. The next day the eruption disappeared, but he felt poorly, and complained of loss of appetite and malaise. Last night, just after going to bed, it suddenly reappeared in the same manner as two days before. The attack was preceded by chilliness and malaise; later he perspired profusely. To-day he feels better, and the rash is leaving the surface. The skin, however, is still red; rough in patches; slightly papular and vesicular, and has the appearance on the arms of an erythema multiforme in the stage of declination; scratch-marks abound. It seems as though the attack had been abortive, the development of the papular and vesicular lesions having been checked early in their course.

16th.—During the past five days the eruption has been disappearing, with slight desquamation and considerable pigmentation, some of the patches on the trunk somewhat resembling irritated tinea versicolor. Within the week a half-dozen, large and small, *pustules* have come on the arms and buttocks, identical with those which have been described.

25th.—A number of variously sized pustules have been appearing here and there over the surface, in particular on the neck, around the navel, on the lumbar and sacral regions, and over the buttocks and thighs. They all incline to dry and crust in the centre, sometimes as a depressed, cup-shaped dust, and to spread on the circumference, thus extending their size. Their edges are more or less "puckered" and slightly raised; their areolæ large, dark red in colour, and retracted, presenting a somewhat stellate, radiate appearance. There is now but little itching. He is still taking four minims of the Liquor Potassii Arsenitis, which he has been using for a month, but with no benefit.

June 29th.—Has been annoyed greatly with disease since the last note, which has manifested itself, as heretofore, in the form of distinct outbreaks appearing at irregular intervals. But at no time within the past three months has

he been entirely free. The lesions at present are *vesicular* and *bullous*, from the size of large pin-heads to coffee-grains, and are scattered especially over face, arms, and forearms, and over the region of the spinal column. They are accompanied with intolerable itching. During the last six weeks he has been using half-ounce doses of linseed meal, with the view of improving the nutrition, but without benefit.

June 1st, 1884.—Five years have elapsed since the last note, during which period I have not seen the patient until a few days ago. He is still suffering with the disease, having never obtained any relief from the manifold treatment to which he has been subjected. For the past three or four years the attacks have been lighter than formerly, and the lesions for the most part vesicular in character. At the present time the face, neck, and trunk are the seat of small, ill-defined vesicles and papulo-vesicles, accompanied, as before, with itching. The general health is improved, and he is able, when not suffering from an attack, to attend to his daily duties.

I shall make no comments upon the case except to say that it illustrates a typical expression of this peculiar disease, characterised as it is by rare multiformity. It shows almost all of the lesions to which I have called attention in describing the disease, and upon which its several varieties have been based. In conclusion, I may add that the affection is usually well defined, having distinctive features which enable it to be readily recognised, although it may be confounded with eczema, herpes, and pemphigus, according to the lesions at hand.

# PRELIMINARY NOTE

ON THE

# RELATION OF DERMATITIS HERPETIFORMIS

TO

## HERPES GESTATIONIS AND OTHER SIMILAR FORMS OF DISEASE.[1]

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In my original communication on Dermatitis Herpetiformis,[2] the symptoms, characteristics, and the several varieties of the disease were described. It was also stated that the pustular variety was the same manifestation as that described by Hebra as impetigo herpetiformis. The view was likewise put forth that the herpes gestationis of authors was probably merely another variety of this affection. In a more recent paper just read before this Association,[3] the relation of the impetigo herpetiformis of Hebra to dermatitis herpetiformis has been shown, and the conclusion reached that the former is but a variety of the latter disease. In the present note I desire to bring forwards supplementary views which have of late been forced upon me by study of the literature of the subject, to the effect that not only the herpes gestationis of writers, but also other similar forms of eruption reported with various titles are all merely instances of one process, namely, dermatitis herpetiformis as I have defined this disease.

To be more definite, some of these cases may be mentioned.

[1] Reprinted from the 'Medical News,' November 22nd, 1884; read before the American Dermatological Association, 1884.

[2] Read before the Amer. Med. Assoc., May 6th, 1884, and published in the 'Journ. of the Amer. Med. Assoc.,' August 30th, 1884.

[3] 'Journ. of the Amer. Med. Assoc.,' August 30th, 1884.

The "herpes circinatus bullosus" of Erasmus Wilson;[1] the "pemphigus prurigineux" of Hardy;[2] the "herpes gestationis" of Milton,[3] Bulkley,[4] Thompson,[5] Liveing,[6] Cottle,[7] Gale,[8] and W. G. Smith,[9] all represent manifestly the same disease, and are expressions of the vesicular and bullous varieties of dermatitis herpetiformis. In like manner the "pemphigus" of Klein;[10] the "pemphigus circinatus" of Rayer;[11] the "herpes phlyctænodes" of Gilbert;[12] the "pemphigus aigu pruriginosus" of Chausit,[13] and the "pemphigus composé" of Devergie.[14] Certain cases of so-called "hydroa" should, I think, also be viewed as forms of dermatitis herpetiformis, as, for example, the cases reported by Handfield Jones[15] and Bulkley,[16] and that of "Florence S.," described in the 'British Medical Journal,' 1870. Likewise such cases as that of Oswald,[17] reported with the heading "a peculiar skin eruption occurring during pregnancy;" and of Leigh,[18] a "bullous eruption of a peculiar character."

The very unusual case of Jarisch,[19] designated "herpes iris," and the case of Meyer,[20] "a fatal pemphigus-like der-

[1] 'Diseases of the Skin,' sixth ed., London, 1867.

[2] 'Leçons sur les Mal. de la Peau,' 2nd part, p. 136, second ed., Paris, 1863.

[3] 'Path. and Treat. of Diseases of the Skin,' London, 1872, p. 205.

[4] 'Amer. Journ. of Obstetrics,' February, 1874.

[5] 'Archives of Derm.,' October, 1875.

[6] 'Lancet,' June 1st, 1878, p. 783.

[7] 'St. George's Hosp. Rep.,' 1879.

[8] 'Lancet,' 1880, vol. i, p. 601.

[9] 'Dublin Journ. Med. Sci.,' 1881, 3 s., lxxi, p. 70.

[10] 'Allg. Wien. med. Zeitung,' August, 1867; quoted in 'Journ. Cutan. Med.,' July, 1868, p. 203.

[11] 'Treatise on Diseases of the Skin,' English translation, London, 1835, p. 219.

[12] 'A Practical Treatise on the Special Diseases of the Skin,' English translation, London, 1845, p. 118.

[13] 'Annales des Maladies de la Peau et de Syph.,' March, 1852.

[14] 'Mal. de la Peau,' p. 309, Paris, 1857.

[15] 'Med. Times and Gaz.,' September 6th, 1873.

[16] 'Archives of Derm.,' April, 1877.

[17] 'Lancet,' June 10th, 1882, p. 951.

[18] 'Lancet,' January 6th, 1883, p. 11.

[19] 'Viertelj. für Derm. u. Syph.,' Hefte 2 u. 3, p. 195, 1880.

[20] 'Archiv für path. Anat. u. Phys.,' November, 1883, p. 185.

matitis," have also points in common with the disease under consideration.

Finally, without doubt some cases of so-called pemphigus, especially of "pemphigus pruriginosus," might more properly be regarded as examples of dermatitis herpetiformis

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## CASE OF DERMATITIS HERPETIFORMIS

WITH

## PECULIAR GELATINOUS LESIONS.[1]

JOHN S—, æt. 64, a native of Wilmington, Delaware, and a pedlar by occupation. He has always enjoyed good general health; weight, 175 pounds. No family history. The present skin disease is of five years' duration, but he has had the same only in winter. It has been in the habit of coming on with cold weather and disappearing about the middle of May, and it has pursued this course every year. He never had any skin disease or illness of any kind before seven years ago, when an "eczema" of the right leg appeared, which has been cured repeatedly by ointments, but has relapsed. He is of the opinion that the disease of the general surface which he now has is the same disease that he has had for the last five years, but that it is worse this winter than ever before. When it first came out (in October, 1874) he was in his usual good health. It manifested itself by intense itching on the back, localised chiefly about the lumbar region, which asserted itself in paroxysms, lasting from a half-hour to two hours. They were invariably relieved in the course of ten or twenty minutes by scratching. Unless scratched or rubbed, itching would persist for hours. The itching was unaccompanied by redness. The scratching did not injure the skin, notwithstanding that he was in the

[1] Reprinted from 'The Medical News,' March 7th, 1885.

habit of employing harsh measures for relief. This pruritus continued all winter, confined to the back, and at no time was accompanied by any eruption. With May it disappeared quite abruptly, as soon, he states, as he began sweating in the course of his pedestrianism. He was entirely well all summer until October, when the disease again began as in the previous year with intense itching without eruption, and confined to the back, occupying, however, more surface than before. It continued all that winter, as during the previous season, and again disappeared in May.

The following October it reappeared, and now for the first time in the form of small, pin-head sized, elevated, inflammatory, acne-like, very itchy pustules, which, after having been emptied, disappeared. They were scattered over the back, and were not grouped. They came at irregular intervals and not in crops. They were present throughout the autumn and winter in varying numbers, and entirely left him in May. The itching was quite as intense as during the two previous years. He states that after these lesions were opened and scratched decided relief was experienced. In October (third year) itching upon the back again manifested itself, which gradually increased in severity, and continued all winter. The small inflammatory, acne-like, pustular lesions which were present during the second winter did not reappear; but toward the middle of April what he describes as small "blind-boil-like" lesions appeared on the back. They neither discharged nor crusted. Two or three came at a time and were very itchy at first, but in the course of two or three days became sore. In the course of the following month there occurred some twenty of these lesions, when, toward the middle of May, they entirely disappeared.

He remained well through the summer, as usual, until October, when the itching confined to the back began as before, unaccompanied by eruption, but a week later the itching began to subside, and now a new kind of lesion appeared, which he describes as follows. When first noticed, two were present over the right scapular region. They were the size of a large thumb-nail, distinctly raised, but flat, with little or no inflammatory areola, of a golden yellow

lour, and contained a thick, consistent, orange or deep lden yellow-coloured mass. These lesions were in many ays peculiar. They came suddenly, often in the course of n or fifteen minutes. His attention would be directed to the fected part by a sharp sensation, "like the sting of a bee;" amining the skin he would find one or more lesions pre- nt, and, as a rule, already fully formed. They were ither preceded by, nor accompanied with itching: the nsation was that of a sting. They were superficially seated, pearing to have their seat just beneath the epidermis. hey would continue "to sting" until opened with a knife needle, a knife being the instrument usually selected for e purpose. (He was at this period an inmate of the Vilmington Almshouse Hospital, and was under the care of r. Thomas Ogle.)

The lesions were too tough to permit of being ruptured ith the finger-nail. He describes them as being circum- ribed, firm but not hard, "puffed up," raised but flat on eir summits, and moveable under the skin. Some were ised as much as a quarter of an inch or more; others less. s soon as he became aware of their existence, by the inging sensation, they were opened; the sting was sharp d persistent until they were evacuated. All of these sions were much alike as to size, shape, colour, and other eneral characters. When opened with a knife, the mass r contents referred to would come out, or "pop out" ntire without any pressure being exerted, and in the form f the pulp and of the consistence of an ox-heart cherry; e mass was, however, flattened rather than round.

These curious, pulpy, gelatinous masses, he states, could e picked up between the fingers, handled, and, if squeezed, ould disintegrate. No blood accompanied them, nor did e cavity which remained after the exit of the mass contain y blood, but it subsequently oozed a few drops of a llowish fluid, of a creamy consistence. A cavity, of course, mained after the exit of these bodies, into which the tip of e index finger could be inserted; but, under a stimulating tion of iodide of potassium, this healed over, with slight aling, in a few days, no stain remaining. Sometimes ese cavities would refill, and often with surprising rapidity,

in less than ten minutes with a material similar to the first product, but not so yellow, and invariably thinner—more of the consistence of thick cream—which could be squeezed out by pressure with the blade of a knife. But not all of the lesions would refill; some would refill as often as three times, and this in from one to twelve hours. He continued to have these very singular lesions throughout the autumn and winter, one, two, three, or more making their appearance, on the average, every day. They did not come in crops, but at irregular intervals, and, as stated, seldom oftener than at the rate of one or two daily. They were at first confined to the back, but subsequently attacked all portions of the surface except the face and scalp.

They disappeared gradually in the following April, and he was free from these and all other lesions throughout the summer.

*Present condition* (January 13th, 1879).—The patient was admitted to the Ward for Skin Diseases of the Philadelphia Hospital on November 1st, 1878, but did not come under my observation until some weeks later. When admitted he presented a slight vesicular and papulo-vesicular eruption, in patches and much scratched, occupying the back, abdomen, and extremities. It appeared to be trivial eczema, although he complained greatly of the itching, declaring that it was intolerable. The case, as stated, was regarded as one of eczema, and was placed upon the usual treatment for this disease. The disease disappeared, in a great measure, in the course of a fortnight, but soon recurred, exhibiting the same characters as before.

December 15th.—An outbreak of vesicular eruption has recently appeared, showing the lesions in a more positive form. They are *vesicles*, varying in size from a small pin-head to a pea, and possess irregular, angular, jagged borders such as are encountered in herpes zoster. Although manifestly inflammatory, they are unaccompanied by marked signs of inflammation, being for the most part altogether without areolæ, though the skin between them is somewhat reddened and excoriated from scratching. They are, as a rule, quite flat, but some are raised, looking as though they might develop into blebs. Their contents are either clear and watery or pale yellowish.

Those which are flat, and contain a clear fluid, are inconspicuous, and even in some places difficult to detect, and resemble sudamina. The lesions show a distinct disposition to form patches, and, moreover, to cluster, and here and there even to run together; but the grouping is not pronounced, and might readily be overlooked by a casual observer. The back of the neck, shoulders, back, arms, and thighs are the regions especially involved, though other parts are also invaded, but with disseminated, abortive, papulo-vesicular, more or less excoriated lesions.

Antipruritic lotions have been freely used, but with indifferent results, an alkaline tarry preparation affording the most relief. The itching has been intense, preventing sleep and causing the patient to scratch incessantly day and night.

The vesicular lesions above described gradually subsided in the course of two weeks, leaving the skin quite free of lesions, except a general dirty yellowish pigmentation, the result of scratching. The patient remained well, except that he was still much annoyed with general itching for a week, when the present lesions, pustular in character, began to appear. They have been very gradually increasing in size, and multiplying from day to day, until the existing condition has been reached.

The lesions are distinctly *pustular*, varying in size from a pin-head to a finger-nail. They are of a yellowish white colour; tensely distended in their early stage; flat; surrounded with marked areolæ; and of irregular, more or less rounded or angular outline, and have a contracted or puckered appearance. The older ones are crusted with a yellowish, slightly greenish, flat, uneven, honeycomb crust. The recent small crusts, in many instances, show a decided umbilicated or cupped formation, reminding one of tinea favosa.

The lesions are numerous, and exist upon the scalp, neck, shoulders, arms, forearms, sacral region, buttocks, thighs, popliteal spaces, legs, breasts, and abdomen. The hands and feet and genitals are almost free. Viewing the eruption as a whole, the lesions may be said to be disseminated, though they are more abundant in some localities than

27th.—The eruption, which threatened to become extensive last week, has again aborted. The lesions were, without exception, all scratched and lacerated almost as soon as they began to form. The itching still continues, but in a modified degree. The officinal sulphur ointment was to-day ordered, to be well rubbed into the skin twice daily.

April 3rd.—The sulphur ointment gave decided and prompt relief, the patient stating that no remedy that he had ever before used had acted so effectually upon the itching.

May 1st.—A few scattered papulo-vesicular and vesicular lesions, accompanied with itching, have shown themselves from time to time during the month, but there have been no signs of a serious outbreak. The patient is improving, he thinks, from week to week, and eagerly looks forward to the approaching warm weather as a source of relief. It will be remembered that every year he has recovered with summer. The internal remedies, consisting mainly of arsenic, have some time since been discontinued. The patient, at his own request, has been discharged from the hospital, and has not since been heard from.

The notes, extending over a period of several years, have been given at length, because the case is very interesting, especially with reference to the "gelatinous lesions" described. At present I shall not dwell on this subject beyond stating that these lesions have likewise occurred in several other instances of dermatitis herpetiformis which have come under my notice. I believe them to be peculiar to this disease, and to constitute a hitherto undescribed form of cutaneous manifestation.

# CASE OF DERMATITIS HERPETIFORMIS

## OF THE PUSTULAR VARIETY.[1]

In reporting the notes of a case of a rare disease no apology therefor need be made, for the reason that any information on the subject must prove valuable. The disease under consideration being of infrequent occurrence, and, moreover, constituting a new field of observation, concerning which there seems to be some diversity of opinion among dermatologists, is for these and other reasons worthy of close investigation. With our present knowledge every case encountered is entitled to a place on record, with the hope that as the published data accumulate we shall better comprehend the process.

The following case was under my observation at intervals during a period of five years. At the time the disease seemed to me incomprehensible, on account of the peculiar lesions, their behaviour and course, which were altogether different from those of any affection with which I was familiar. Classification of the disease was beset with difficulties, as the original notes testify, and the case was regarded as an anomalous one—as representing, perhaps, an undescribed disease. The several provisional diagnoses (of eczema ? of ecthyma ? of tinea circinata ?) made from time to time show the resemblance of the lesions to those of well-known affections, and give an idea of the multiformity displayed. The case, moreover, is interesting as exhibiting a phase of this peculiar disease that has not been brought out in any of the cases that I have previously reported. These features will be referred to later.

[1] Reprinted from the 'Medical News,' March 5th, 1887.

The patient came under notice in 1874, and the following history is an abstract of the notes taken at that date. Daniel Welsh, fifty years of age, Irish, and an ostler by occupation. He had previously been subject to "prickly heat" during the summer about the trunk, and was so affected year before last, this attack having been followed by a much more serious disease of the skin similar to that, he states, with which he now suffers. He describes the eruption he had at that date as being pustular and vesicular, with intense itching and burning. The itching was intolerable, and the disease continued for three months. Crusting followed the formation of the pustules, which remained for some time, the process eventually passing off with scaling. He recovered in the autumn, and remained well six months, when the present eruption appeared. It continued throughout the summer, becoming better toward autumn, but it never left him entirely.

About a month ago it began to grow worse. It is now confined to the trunk, shoulders, and buttocks, and is particularly well defined upon the abdomen and sides of the thorax. The lesions are disseminated, but possess certain herpetic features, and consist of numerous minute, small and large pustules with yellowish contents, in all stages of development. They vary much in size, some being no larger that pin-points and pin-heads, while others have attained the size of peas and beans. The latter are not acuminated, but are flat and spread out, although considerably raised above the surrounding healthy skin. In outline the larger ones, as a rule, are oblong or irregular and angular, and have an herpetic, "puckered" appearance. The small recent pustules are not attended with any redness of skin, having no inflamed base or areola; but the larger and older ones are surrounded with a deep red areola of considerable size. There are no vesicles. [A week's observation proved that this eruption began as a well-defined pustule, and continued as such until a crust formed, which became detached in four or five days, leaving a pigmented base.] In addition to the pustules there is considerable pigmentation, of a reddish, dirty yellowish, brownish hue, which is present here and there over the surface in a marked degree, and is a conspicuous symptom,

much greater and more persistent than with other inflammatory processes.

disease at present is almost without itching, burning, r annoying symptoms. The eruption, he states, comes crops, one scarcely disappearing before another makes earance, and in this manner the process is kept up from o week and month to month.

h was the condition when admitted to the Dispensary in Diseases, April 28th, 1874. He was placed upon al and internal treatment, the disease being then ed as pustular eczema. During the following month, the use of iron and arsenic and varied external es, the cutaneous lesions increased. A few weeks later pustules began to appear in a grouped, circinate, ic form, as in typical tinea circinata, the appearances ling an exaggerated phase of this latter disease, so so that it was thought it might possibly be due to a ble parasite, but the microscopic examination revealed g of this nature.

ing and heat now began greatly to annoy the patient, thin a week some of the circinate patches increased until they became two inches in diameter. The es were minute and small, and hence the picture did ggest herpes iris. Two weeks later the attack sub- and the lesions rapidly disappeared, but only to re- immediately as a new crop as before, in the form of ous pin-point and pin-head sized pustules. The ng week another crop, numbering thousands of lesions, d the trunk, accompanied with burning but no itching. ttack increased in extent and severity, but the lesions ed small, a few only being as large as a pea. Scales in crusts formed in large patches, and scaling and ex- n set in. The skin became intensely itchy and hot, and unable to sleep, and was depressed and discouraged. patient now passed from under observation, having enced no relief from the varied treatment which he dergone. Five years afterwards he again presented f to me, still a sufferer with the same disease. An nt containing sublimed sulphur one ounce, lard two , and oil of walnuts two drachms, was now used, and

with positive relief to the itching and burning, and with the remarkable result of causing the lesions rapidly to disappear. The inunctions were made with friction, as in the treatment of scabies. I subsequently saw him in several attacks, in one of which the pustules were herpetic and grouped, as previously, in a crescentic or more or less annular form, new lesions, moreover, showing themselves on the periphery of the patches, accompanied with much itching. The ointment referred to was again (and on later occasions) employed with the same admirable result, the patient stating that during the many years of his suffering this was the first and only remedy that had in any degree benefited him. He spoke of the relief to the subjective symptoms as being instantaneous, and looked forward to a speedy permanent cure. Whether or not this occurred I am unable to say, as shortly afterwards he ceased attending the clinic.

The interesting points of this case are, first, that during the period I had the patient under observation the lesions remained pustular, being at times minute (not larger than pin-points and pin-heads), and on other occasions larger—the size of peas and beans. At all times, even when the eruption might be regarded as being disseminated, they possessed herpetic features, being either (when of large size) seated upon an angry-looking, drawn-up, puckered base, or (when small) grouped in close proximity, sometimes in an annular form, as in tinea circinata and herpes iris. As characteristic of the disease may be mentioned the disposition of the eruption to appear in crops ; the pigmentation of the affected skin ; the obstinacy of the process to treatment; the tendency to relapse ; and the long duration of the disease as a whole. Finally, the subjective symptoms were peculiar, being at one time marked and at another time almost absent. The variations on this point were remarkable if the statements of the patient are to be relied on. The fact, however, of the lesions being pustular would account for the comparative freedom from itching, this symptom, as is well known, rarely accompanying pustular lesions of any kind.

# CASE OF DERMATITIS HERPETIFORMIS

## RESEMBLING ERYTHEMA MULTIFORME.[1]

In January, 1884, I was requested by Dr. Mitchell of Elkton, M.D., to see a case of chronic cutaneous disease, exhibiting peculiarities which made the diagnosis difficult. The patient was a man seventy years of age, a lawyer by profession, neurotic and in poor general health.

The disease had existed a year or longer, and was characterised by a profuse, multiform, general eruption, with violent itching and burning. None of the various plans of treatment previously employed had afforded any relief.

From his physician I further learned that the lesions of the skin had varied in character from time to time, having been sometimes vesicular, and on other occasions erythematous; while more frequently there had existed a combination of these elementary forms. Itching had always been a marked feature.

When I first saw the case the whole general surface was the seat of an abundant, diffuse eruption, characterised by ill-defined, marginate, annular, and circinate erythematous patches, upon which, in many places, were more or less well-formed, variously sized and shaped papulo-vesicular and vesicular lesions. The skin showed, moreover, signs of subacute and chronic inflammation, in the form of thickening, pigmentations, excoriations, and blood-crusts, as well as lesions in all stages of development. The erythematous patches predominated, and had coalesced to such an extent that their outline was only in places defined, but everywhere could be seen a disposition to form marginate shapes, as in erythema

[1] Reprinted from the 'Medical Record,' April 2nd, 1887.

multiforme. The patches were on a level with the surrounding skin or were slightly elevated, and were acutely congested and infiltrated with inflammatory products, partly plastic and partly serous in nature. In colour they were bright red or violaceous red, according to their age, and were mottled, owing largely to the fact of their having run together. The whole general surface, but especially the trunk, was affected in this manner; in addition to which seated upon these patches were, for the most part, flat, small and large papulo-vesicular and vesicular lesions, here and there well defined, elsewhere imperfectly developed or abortive. The picture, as might be imagined, suggested an extensive diffuse or generalised "chronic" erythema multiforme, with papulo-erythemata, papulo-vesicles, and vesicles. The herpetic element was striking, as shown by the grouping and by the marginate peripheral extension of the process. Here and there the lesions were grouped in an ill-defined circinate form, as in tinea circinata, some of the patches being small, others large. In most localities they were so multiform and had emerged one with another so extensively that the elementary characters were to be noted only on close inspection. Scratch-marks, excoriations, and small and large blood-crusts were everywhere present, testifying to the intense itching which had been experienced. The patient stated that this had always been a distressing symptom, was subject to exacerbations, and that it was always at its height during the time a new crop of lesions were developing, occupying usually about a week. The pigmentation was of a dirty yellowish, muddy, or dusky hue, and was both localised and general. It called to mind that seen in the later stages of extensive pityriasis rosea of the trunk.

From a diagnostic standpoint the eruption resembled diffuse, aggravated erythema multiforme of long standing. Herpes iris was not suggested, the erythematous element prevailing. It possessed a history, however, as well as features which precluded it from being classed here. The chronicity of the process, the tendency to repeated relapses, the obstinacy of the disease, together with the violent itching and burning, would not permit it to be considered as a case of this disease, at least as this affection is now

ned. At the same time I would state that the case ɜessed certain features in common with this disease, and ainly bore more resemblance to it than to any other l-known cutaneous disease. And this brings me to a stion that has presented itself on several occasions in lying dermatitis herpetiformis, namely, where (in cer- ı cases) shall the line be drawn separating this disease n other well-defined diseases? Shall, for example, the e I have just cited be regarded as erythema multiforme, shall it be grouped under the title dermatitis herpeti- nis, where I have placed it? Shall a new definition be ned for erythema multiforme, to include also a *chronic* cess, in order that this and similar cases may be grouped ler this title; or shall we regard such instances as too removed from erythema multiforme to be classed here, l relegate them to another group? The line separating disease of the skin from another in some instances is defined, and there are cases occasionally encountered ich may as properly be classified under one head as ɔther.

Instances of the kind are met with from time to time h eczema and psoriasis, pityriasis rubra, and psoriasis, l, to pass to more chronic forms of inflammation, with us erythematosus and lupus vulgaris. They exhibit nptoms common to both diseases, and defy precise sche- tic classification.

The case under discussion, however, I think, may more ɔperly be regarded as an example of the erythematous iety of dermatitis herpetiformis than of erythema multi- me, especially if we take into consideration the history of disease. In some respects it resembles that reported by risch as "herpes iris," and referred to by me in the icle entitled "Preliminary Note on the Relation of Derma- is Herpetiformis to Herpes Gestationis and other Similar rms of Disease" ('Medical News,' November 22nd, 1884). I saw the patient on several occasions during the subse- ent six months, his condition having somewhat improved, hough he still suffered much. It is not necessary to enu- rate the various internal and external remedies that re employed; suffice it to say that they were such as

might have been prescribed for chronic universal erythematous eczema. Notwithstanding the treatment the disease persisted, and relapses, though milder in form, occurred as before.

I report the case because it is interesting as portraying an unusual manifestation of the disease, namely, one bearing a resemblance to erythema multiforme. In a former paper I alluded to the possible relationship between these two diseases, and this case would go to show that the causes at work in these diseases are capable of giving rise to similar cutaneous lesions. Additional clinical information, however, is needed concerning unusual forms of both diseases before definite views can be expressed, and it is to be hoped that the experience on this point of other dermatologists will be forthcoming.

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## ÜBER DIE DIAGNOSE DER DERMATITIS HERPETIFORMIS.[1]

Bei der Durchsicht der Berichte über bestimmte, von Zeit zu Zeit in den letzten Jahren veröffentlichte Fälle von Hautkrankheiten sowie auf Grund der verschiedenen mir bekannt gewordenen Kritiken und Referate über meine Abhandlungen über Dermatitis herpetiformis dürfte es scheinen, als ob die Krankheit von einigen nicht deutlich aufgefasst worden ist. Nach den Verhandlungen der New Yorker Dermatologischen Gesellschaft, in welcher dieses Thema diskutiert wurde ('Journ. Cutan. and Ven. Dis.,' April, 1886, p. 20) deuten die Erörterungen wohl darauf hin, dass nicht alle Mitglieder mit den verschiedenen Phasen der Affektion vertraut waren. Die hierbei zu tage

[1] Vortrag, gehalten vor der American Dermatological Association auf der 11 Jahresversammlung am 1 September, 1887.

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getretenen Ansichten beweisen die über diesen Gegenstand herrschende, grosse Meinungsverschiedenheit. Aus diesen und andern Gründen wünsche ich Ihre Aufmerksamkeit nochmals auf dieses Thema zu lenken, indem ich speziell die charakteristischen Merkmale und Symptome der Affektion, durch welche sie sich von andern ähnlichen Dermatosen unterscheidet, in Erwägung ziehe.

Mein erster, 1884 publizierter Artikel über diese Krankheit gründete sich auf die Erfahrung, welche ich bei einer Anzahl von mir ab und zu beobachteten Hautaffektionen mit gewissen, allen gemeinsamen Merkmalen gewonnen habe. Diese Manifestationen schienen mir auf demselben Prozess zu beruhen und sollten daher zusammengefasst und unter einem Namen erörtert werden. Die damals aufgestellten Ansichten sind, wie ich glaube, auch jetzt noch der Hauptsache nach korrekt, sicherlich soweit sie die klinischen Studien betreffen. Da einige dieser Fälle viele Jahre unter meiner Beobachtung waren, hatte ich während dieser Zeit reichlich Gelegenheit die verschiedenen Eruptionsphasen und den Prozess als ein Ganzes zu studieren. Seitdem haben andre Beobachter über Fälle derselben Krankheit berichtet, und ist daher zu erwarten, dass wir bald über hinreichendes Material verfügen, um präziser definieren zu können, welche Fälle unter obigem Namen zu rubrizieren, und welche andern wohlbekannten oder schon anderweitig untergebrachten Krankheiten zuzuweisen sind.

Über die Existenz einer Krankheit "Dermatitis herpetiformis," wie sie spezieller durch Varietäten von Bläschen, Blasen und Pusteln charakterisiert wird, hege ich keinen Zweifel. Der Zweck meines heutigen Vortrages geht dahin, die typische oder gewöhnliche Bezeichnung der Affektion zu erörtern. Denn es ist ausserordentlich wichtig, sich über diesen Punkt völlig zu verständigen. Über die allgemeine oder gewöhnliche Form der Erkrankung muss vor allem Übereinstimmung bestehen, erst dann können die verschiedenen Abweichungen von diesem Typus berücksichtigt und an ihre richtige Stelle gebracht werden, je nachdem die Erkenntnis derselben fortschreitet. Meine Erörterungen werden sich demnach nur auf die gewöhnliche Erscheinungsform der Krankheit beschränken.

Nach diesen einleitenden Bemerkungen mögen bestimmte allgemeinere Punkte hervorgehoben werden. Vor allem ist es für die Auffassung des Gegenstandes wesentlich, bei einer ihrem Charakter nach so polymorphen Affektion die einzelnen Varietäten und pathologischen Formen derselben in Erwägung zu ziehen. Im Ekzem z. B. haben wir eine Krankheit vor uns, welche mit verschiedenen Arten von elementaren Effloreszenzen und in verschiedenen Varietäten beginnen kann und dann einen von jeder andren Dermatose differierenden Verlauf nimmt. Ohne hinreichende klinische Erfahrung bezüglich dieser Affektion wird niemand imstande sein, die zahlreichen und besonderen Phasen, welche sie während ihrer Entwickelung annehmen kann, zu würdigen. Die meisten von mir beobachteten Fälle hatten einen noch wechselvolleren Charakter als das Ekzem. Vielleicht ist gerade die Polymorphie des Exanthems, wie sie sich im Verlauf des natürlichen Prozesses manifestiert, ein Hauptcharakteristikum,—bald in Form von Bläschen, bald Blasen oder Pusteln, ja in einer oder mehr Eruptionsperioden bestehen alle diese Formen gleichzeitig und bilden eine reine Mischeruption. Und gerade wegen dieser charakteristischen Eigentümlichkeit, welche in bestimmten Umfang in fast allen Fällen verhanden ist, ist es zum Verständnis des Prozesses als eines einheitlichen wesentlich, den Patienten unter fortgesetzter Beobachtung zu haben. In bestimmten Fällen ist es leicht erklärlich, wie zu einer Periode ein vesikulöses Ekzem, ein oder zwei Monate später irrtümlicherweise ein Pemphigus diagnostiziert werden kann. Doch kann es als feststehend erachtet werden, dass gegebenen Falles während einer genügend langen Beobachtungsdauer die Polymorphie des Exanthems in einer oder der andren Eruptionsperiode früher oder später sich offenbart, sowie dass diese Eigentümlichkeit in verschiedenen Intervallen und dazu wei bei keiner andren Krankheit sich wiederholen wird. Die typische Form zeigt sich in der Produktion von Bläschen, Blasen und Pusteln, die entweder gleichzeitig auftreten, also eine Mischeruption bilden, oder zu verschiedenen Zieten als mehr oder weniger deutlich charakteristisch vesikulöse, bullöse oder pustulöse Eruptionen. Die gewöhnlichste und häufigste Form ist die Mischeruption mit

vorherrschend vesikulösem Typus. Als gute Beispiele dieser Art mögen die beiden in dem ‘New York Med. Journ.,’ April 9th, 1887, erörterten Fälle erwähnt werden; ferner die Fälle von Mrs. N. P. (‘The Medical News,’ June 2nd, 1883), sowie von H. H. Mck. (‘New York Med. Journ.,’ November 15th, 1887); in diesen Fällen bestanden Bläschen, Blasen and Pusteln gewöhnlich gleichzeitig, doch prävalierte stets die vesikulöse Form. Diese Beispiele repräsentieren, den sogenannten Herpes gestationis von Milton, Bulkley und andern, während über ähnliche Fälle unter andern Titeln von Zeit zu Zeit berichtet worden ist.

Als ich meine Ansichten über diese Krankheit ursprünglich darlegte, schien es mir ratsam, zur möglichst klaren Darstellung eines so komplizierten Themas die gewöhnlichen Phasen der Affektion unter dem Titel von Varietäten zu beschreiben, welche sich auf die vorherrschenden Elementarformen in ähnlicher Weise wie bei den Varietäten des Ekzems zurückführen lassen. Denn man muss bedenken dass zwar der Prozess zum gleichzeitigen Ausbruch von zwei und mehr Exanthemformen inkliniert, aber doch auch Fälle nicht fehlen, in denen bei der einen oder andren Eruptionsperiode nur eine Art von Ausschlag vorhanden ist. So bestanden in verschiedenen meiner Fälle für längere oder kürzere Zeit nur Bläschen, später kamen während eines Recidivs Blasen oder Pusteln zum Vorschein. Wie es schien, lag für die Annahme von Varietäten kein Grund vor, sie bestanden in erythematösen, vesikulösen, bullösen, pustulösen, papulösen und klinisch in polymorphen Formen. Die erythematöse Form ist charakterisiert worden durch den Fall des Advokaten aus Maryland Mr. Mcl. (‘Med. Record,’ April 2nd, 1887). Die Fälle von N. B. E. (‘New York Med. Journ.,’ July 10th, 1884) sowie von Capt. K. (‘Amer. Journ. Med. Sci.,’ January, 1885) zeigen beide in ausgesprochenem Grade die bullöse Form, während die pustulöse Varietät sich in den Fällen von Annie Mcl. (‘Journ. Cutan. and Ven. Dis.,’ vol. xi, No. 8) und von Daniel Welsh (‘Med. News,’ March 5th, 1887) manifestierte. Ein Beispiel der polymorphen Art bot sich in dem Falle von Mrs. M. (‘Med. News,’ July 19th, 1884) dar, bei welchem für eine geraume Zeit alle Phasen und

Stadien von primären und sekundären Eruptionsformen in solcher Ausdehnung bestanden, dass eine Schilderung kaum eine genügende Vorstellung von dem vorhandenen Bilde erwecken würde.

Lassen Sie mich hier auf eine kurze Schilderung der charakteristischen Symptome der Krankheit eingehen. Es kann die Frage gestellt werden, ob sich bestimmte Charaktere finden, durch welche die Affektion von andern Erkrankungen unterschieden werden kann, ferner ob die Symptome eide eigenartige Affektion kennzeichnen, oder ob dieselben nur ungewöhnliche Formen gewisser, wohlbekannter Affektionen darstellen, wie z. B. des Erythema multiforme oder des Pemphigus. Besitzen wir ferner genügende Thatsachen und Beobachtungen, auf Grund welcher wir eine Schilderung einer eignen Erkrankung entwerfen können? Die letztere Frage kann nach meiner Meinung positiv beantwortet werden. Zur näheren Erörterung des Gegenstandes darf hervorgehoben werden, dass es nicht nur wohlcharakterisierte primäre Eruptionsformen verschiedener Art gibt, sondern dass auch sichere, offenbar abortive Formen eine augenfällige Rolle spielen. Zur Erläuterung meiner Ansicht über die letztere Art möchte ich die mangelhaft entwickelten Papeln und papelähnlichen Bläschen anführen, wie man nie nicht selten beim Herpes Zoster trifft. Zu den primären Manifestationen gesellen sich sekundäre Eruptionsformen, welche bei chronischen Fällen ein ganz bestimmtes Bild darbieten. In Fällen mit vorwiegend erythematösen Effloreszenzen sind die Eruptionen weniger gut ausgesprochen, es finden sich mehr oder weniger in Kreisform angeordnete, kleine oder grössere Flecke, auch Entzündungsherde, und auf denselben entstehen undeutlich abgegrenzte, erythematös-vesikulöse Formen oder flache auch zerstreute Bläschen resp. bläschenartige Eruptionsformen; dieser Umstand hat einigen Autoren Veranlassung gegeben, ein "Erythema vesicans" zu beschreiben. Ein ähnlicher, wenn nicht damit identischer Zustand findet sich zuweilen in den vorgerückteren Stadien des Erythema multiforme.

Hinsichtlich der Gestalt und Grösse der andern Eruptionen herrscht die grösste Verschiedenheit. Zuweilen

nd die Bläschen sehr klein, von Nadelkopfgrösse, in esem Fall sind sie in der Regel sehr zahlreich; zuweilen ieder sind sie viel grösser und im allgemeinen variieren sie nsichtlich des Umfanges bedeutend. Ihre Umrisse sind regulär, gezakt oder sternförmig und haben rundliche oder rale Form, dazu haben sie die Neigung sich abzuflachen nd sich eher auszubreiten als zu erheben. Dieser Umstand ägt dazu bei, dass die kleineren Bläschen nicht selten hwer zu entdecken sind und gewöhnlich erst bei schräger eleuchtung sichtbar werden. In der Regel sind sie prall espannt und haben deshalb einen perlenartigen Glanz; urz, sie sind herpetisch. Sie erscheinen auf unbestimmt egrenzten, unregelmässig gestalteten und ausgedehnten lecken, oder sie stehen dicht beisammen oder sind mehr der weniger deutlich gruppiert. Dieselben allgemeinen haraktere finden sich bei den Blasen. Die Pusteln sind ntweder wie bei den Bläschen klein und zahlreich, wie eine iliare Eruption auftretend, oder sie sind von Erbsengrösse nd grösser, in welch letzterem Falle sie wieder spärlich orhanden sind. Die miliaren Eruptionen verhalten sich igentümlich, sie sind flach, gelblich oder weiss, erheben ich auf unregelmässig gestalteten oder kreisförmigen lecken und verleihen zuweilen der Oberfläche ein Aussehen, ls wäre sie mit Punkten oder Knötchen besät. Sie sind n allgemeinen isoliert. Die grösseren Pusteln von rbsengrösse zeigen in der Regel einen Entzündungshof, nd flach oder wenig erhaben, haben eine entzündlich rscheinende Basis, ein etwas gerunzeltes und gefaltetes ussehen, wie es bei den isolierten Effloreszenzen des erpes Zoster gefunden wird.

Die Papeln, welche zuweilen auftreten, sind gewöhnlich reit, so gross wie kleine Spliterbsen und erscheinen als nvollkommene Eruptionen, zeigen aber einen deutlich herpeischen Charakter und gleichen den Papeln des Abortivosters. Hinsichtlich der sekundären Effloreszenzen ist zu emerken, dass eine unrein gelbliche oder bräunliche Pigmentierung in chronischen Fällen im allgemeinen ein vorherrschender Typus ist, viel mehr noch als das bei einem Ekzem on ähnlicher Vielgestaltigkeit und Ausdehnung der Fall st. Krustenbildung kann als ein Charakteristikum nicht

angesehen werden, doch treten gewöhnlich infolge Kratzens Exkoriationen zusammen mit beträchtlicher Verdickung der Haut auf.

Nach dieser kurzen Betrachtung der auffallendsten Eigentümlichkeiten der Effloreszenzen will ich das Gesamtbild, welche sie darstellen, erläutern. Die verschiedenen bereits erwähnten Kombinationen bilden eine hervorstechende Eigentümlichkeit der Affektion. Bei keiner andren Hautkrankheit trifft man so sonderbare Kombinationen, z. B. Erythem, Bläschen und Blasen; Bläschen und Blasen; Bläschen, Blasen und Pusteln; oder Bläschen und Pusteln, welche häufig ganz nahe beieinander stehen, und von stärkerer oder geringerer Pigmentierung, ferner von Exkoriationen und andern sekundären Veränderungen gefolgt sind. Auch der subjektiven Symptome geschehe hier Erwähnung. Jucken und Brennun, besonders in Anfang, sind gewöhnlich in hohem Grade vorhanden. Diese Erscheinungen sind im allgemeinen sehr quälend und zeigen sich bei jeder Exacerbation oder neuen Eruptionsattacke. Dem Drange zum Kratzen können die Patienten nicht widerstehen und bekommen erst Linderung, wenn die Effloreszenzen völlig zerkratzt sind. Das intensivste Jucken veranlafst die vesikulöse Varietät; bei der pustulösen Form sind die subjektiven Symptome im allgemeinen milder, können sogar für kürzere oder längere Zeit gänzlich fehlen.

Wiederholt ist die Aufmerksamkeit auf die Eruption an sich, betrachtet als ein Ganzes, als herpetisch, gelenkt worden. Es ist von Wichtigkeit in eine genaue Präzisierung des Begriffes dieser Bezeichnung einzugehen. Was bedeutet der Terminus "herpetisch." Es kann wohl festgestellt werden, dass derselbe sich auf gewisse Eigentümlichkeiten der Effloreszenzen bezieht; einen ätiologischen Gesichtspunkt involviert derselbe aber in keiner Weise. Unter dem Ausdruck "herpetiform" ist die Ähnlichkeit zu verstehen, welche die verschiedenen als Herpes bekannten Effloreszenzen untereinander haben, dazu gehören der einfache und febrile Herpes, Herpes Zoster und Herpes iris.[1] Bei all diesen Affektionen treten sogenannte herpetische

[1] 'Anm. d. Übers.' Engländer und Amerikaner bezeichnen Herpes tonsurans nicht als Herpes, sondern als Tinea trichophyt., Ringworm.

Charaktere auf, und doch sind sie nicht alle untereinander gleich. So sind die charakterischen Momente beim Herpes Zoster sehr verschieden von denen des Herpes iris, trotzdem aber gibt es wieder andre Eigenschaften, welche beiden gemeiusam sind und zu der ganzen Gruppe gehören. Spricht man von einer herpetiformen Krankheit, so liegt gewiss der Gedanke fern, dass dieselbe einer Varietät von Herpes mehr ähnelt als der andren, oder mit andren Worten, dass sie eine besondere Varietät von Herpes bildet, dass sie vielmehr gewisse der Gruppe gemeinsame Merkmale besitzt.

Hier ist zunächst das dichte Beieinanderstehen, die Anhäufung ung Gruppierung zu erwähnen, welche beim Herpes Zoster am ausgesprochendsten sind. Eine Tendenz zur Gruppenbildung wird auch bei Herpes iris beobachtet, doch in geringerum Grade, es besteht hier aber noch eine andre eigentümliche Neigung, nämlich die Disposition, an der Peripherie in mehr oder weinger ausgesprochener Kreisform allmählich sich weiter zu verbreiten. Dieselbe Tendenz findet sich auch bei einer ihrer Natur nach ganz davon verschiedenen Krankheit, nämlich der Tinea circinata parasitica, die früher der Herpesgruppe zugerechnet wurde—dem Herpes circinatus alterer Dermatologen. Blasenbildung, sogar oft typische, zeigen alle Formen von Herpes, und bei Herpes Zoster ist auch Pustelbildung die gewôhnliche Form.

Es besteht noch ein andres herpetisches Kennzeichen, das man bei allen Varietäten wiederfindet, es ist dies die ausserordentliche Hartnäckigkeit der Effloreszenzen, die fehlende Disposition zur spontanen Ruptur derselben.

Ein variabler Grad von Entzündung ist allen Herpesaffektionen eigen, am wenigsten ausgeprägt ist er beim einfachen Herpes, am meisten beim Herpes Zoster und iris.

Bei Herpes des Gesichts sind die Effloreszenzen in der Regel kalt, d. h. sie zeigen nur einen geringen Entzündungshof, die Bläschen schiessen plötzlich von der Oberfläche auf und sind von keiner grösseren Störung der umgebenden Haut begleitet. Beim Herpes der Schleimhäute und Übergangsstellen ist die Entzündung gewöhnlich viel mehr ausgesprochen. Beim Zoster ist dieses Symptom, wie bekannt, im allgemeinen ausserordentlich stark und überdies eigentümlicher Art, umschrieben, intensiv um die Bläschen

herum, und verleiht der ganzen Eruption oder Eruptionsgruppe ein etwas erhabenes (reliefartiges) Aussehen, welches um ainzelne Effloreszenzen und kleine isolierte Gruppen besonders deutlich ist. Derselbe Zustand findet sich in viel geringerer Ausdehnung bei Herpes iris ; aber hier zeigt sich ein andres herpetisches Merkmal, nämlich die periphere Ausbreitung, in Form von einer oder mehreren Reihen von mehr oder weniger wohlbegrenzten Ringer von Effloreszenzen, insofern die zuerst im Zentrum des Fleckes gebildeten einer Involution unterliegen. Derselbe Entwickelungsprozefs findet in geringerer Ausdehnung bei Tinea circinata statt, und erscheint es mir daher wahrscheinlich, dass die Art der Hautnervenirritation, wenn auch verschiedenen Ursprungs, doch in beiden Erkrankungen ähnlich ist ; das klinische Bild und die Entwickelung der Krankheit würde sicherlich einer solchen Schluss rechtfertigen.

Es wird demnach klar werden, dass der Ausdruck herpetiform mehr als einen Begriff in sich schliesst ; er deutet auf verschiedene Modifikationen von Effloreszenzen, die in ihrer Form ganz verschieden sind. Beim Zoster folgt die Eruption offenbar dem Verlauf eines Nervenstammes-astes odorfadens. Bei den andern Varietäten lässt sich eine so ausgesprochene Beziehung zu den Nerven nicht nachweisen, obwohl hier nach meiner Meinung Grund zu der Annahme vorliegt, dass die Hautnerven affiziert sind, sowie dass eine eigentümliche Art von Nervenstörung die direkte Ursache der Eruption ist. Eine weitere Klärung erreicht man durch Berücksichtigung des natürlichen Verlaufes.

Viele Beobachtungen sind zu machen, wenn man den natürlichen Verlauf der Krankheit verfolgt ; er ist eigentümlich und voh dem jedes andren Prozesses verschieden. In der Regel zeigt die Affektion einen deutlich chronischen Verlauf, der sich über viele Jahre erstreckt. Ich habe über zwei Fälle referiert, wo dieselbe elf resp. dreizehn Jahre bestand und ohne Aussicht auf Heilung noch florid war ; in andern Fällen litten die Patienten ein bis fünf Jahre daran. Es sind mir auch Beispiele erinnerlich, in denen die Affektion nur wenige Monate dauerte, dies betrifft gewöhnlich Frauen während der Schwangerschaft, die Eruption trat von der Entbindung auf und endigte kurz

achher, wie es z. B. bei Mrs. N. P. (‘The Med. News,’ June , 1883) der Fall war. Es besteht nach allem eine sehr ebhafte Tendenz zur Chronizität und zwar trotz lokaler und aterner Therapie, die in vielen Fällen nutzlos ist.

Ein andres Charakteristikum kann erwäht werden; es esteht darin, dass die Eruption in Form von mehr oder veniger deutlich abgegrenzten Anfällen auftritt; jeder lauert zwei bis sechs Wochen, dann folgt wieder ein fast völliger Stillstand für Wochen und Monate. Recidive von gewöhnlich kurzer Dauer zu verschiedenen Perioden bilden die Regel. Eine andre eigentümliche Erscheinung während der Entwickelungsperiode der Krankheit besteht darin, dass eine bestimmte Regel in der Manifestation der verschiedenen Arten derselben nicht befolgt wird. So kann gegebenen Falles die erste Effloreszenz vesikulös und bullös sein, die folgende pustulös, während zu einem späteren Zeitpunkt Bläschen, Blasen und Pusteln gleichzeitig bestehen können, und solche Variationen können bis in infinitum erfolgen. Ich habe mir die Mühe genommen meine referierten Fälle auf diesen Punkt zu prüfen und finde, dass bei Capt. K. (‘The American Journal of the Medical Sciences,’ January, 1884) zuerst Bläschen auftraten, denen am sechsten Tage Blasen folgten; der zweite Ausbruch kurze Zeit nachher war pustulöser Natur, der dritte vesikulöser, bullöser, vesiko-bullöser und pustulöser, der vierte vesiko-pustulöser Art und so fort. In einem andren, lang dauernden Falle (13 Jahre und mehr), dem des H. H. Mck. (‘New York Med. Journ., November 15th, 1884) ist die Krankengeschichte folgende; zuerst Erythem oder Urticaria, dann Pusteln; das dritte Recidiv war vesikulös und bullös; das nächste vesiculös und pustulös; die folgenden Attacken waren vesiko-pustulös, vesiko-papulös, pustulös, erythematös, pustulös, vesikulös und bullös, und vesikulös, und so weiter, so dass man endlich müde wird die vielen und kapriziösen Veränderungen aufzuzeichnen.

Meinen Studien nach will es mir scheinen, als ob der Prozess eine regelmässige Reihenfolge in der Manifestation der Effloreszenzen nicht innehält; es besteht hier eine ausserordentliche Variation, und das ist ein so gewöhnliches Merkmal bei der Entwickelung des Prozesses, dass es als

ein charakteristisches angesehen werden kann. Es kann anderseits von einigen Beobachtern der Einwand gemacht werden, dass ein ähnlicher Verlauf auch bei langdauernden Ekzemen sich findet, indessen sind hier die Variationen von einer zur andren Eruptionsform selten so rapid und scharf abgegrenzt wie bei der hier erörterten Affektion.

Hinsichtlich der Entwickelung und Involution der einzelnen Effloreszenzen ist zu erwähnen, dass dieselben sich von denen andrer, ähnlicher Affektionen unterscheiden. Sie entwickeln sich in der Regel mit ziemlicher Schnelligkeit, wenige Tage oder eine Woche genügen im allgemeinen zur Ausbildung der vollen Eruption; neue erscheinen fortwährend in einer odor zwei Wochen, tritt dann ein Nachlass der Eruptionen ein, so sind die ersten inzwischen schon in weiter Ausdehnung verschwunden. Beginnt einmal ein Nachlass, so geht die ganze Affektion gewöhnlich schnell zurück.

Nach dem Gesagten ist die Krankheit als eine ernste aufzufassen, und so ist es. Denn abgesehen von dem chronischen Verlauf und der Hartnäckigkeit des Prozesses sind die Attacken im allgemeinen sehr quälend nicht nur hinsichtlich der Anwesenheit einer so unangenehmen Eruptionsform an sich, sondern auch wegen des unerträglichen Juckens und Brennens. Solche Patienten können überdies für Wochen und Monate an das Bett gefesselt sein, noch kann man vorhersagen, wie ihr Zustand sich von Monat zu Monat gestaltet. Die Gegenwart oder Abwesenheit von Allgemeinstörungen, Schüttelfrösten und Fieber, wei bei Malaria, wird hauptsächlich von der Schwere des Falles sowie von der Natur des wirksamen Agens abhängen. So können z. B. bei Schwangeren selche Allgemeinsymptome in erhöhtem Grade vorhanden sein. Anderseits können sie in einfacheren Fällen von verschiedenen Ursachen, wie z. B. von nervöser Depression oder vom Shok ahhängen und dann nur leicht sein, auch können sie völlig fehlen. Sind sie vorhanden, so machen sie sich bei jeder Exacerbation besonders bemerkbar.

Diagnose, Anamnese, Verlauf, Verteilung, Entwickelung der Eruptionen, ihre verschiedenen Kombinationen und Eigentümlichkeiten in Verbindung mit den subjektiven Symptomen müssen sämtlich in Erwägung gezogen werden.

Meist ist die Diagnose bei gewöhnlicher Untersuchung leicht zu stellen, in manchen Fällen ist eine längere Beobachtung erforderlich. Die Entwickelung des Prozesses muss stets ein wichtiges Moment bilden und in allen Fällen berücksichtigt werden.

Welche Beziehungen bestehen nun zwischen Dermatitis herpetiformis und andern wohlbekannten Hautkrankheiten? Ist sie eine ungewöhnliche Art irgend einer der andern bekannten Affektionen, oder hat dieselbe besondere, eigne Merkmale, und kann ihr demgemäss in dem System der Hautkrankheiten eine besondere Stelle eingeräumt werden? Sind die sie charekterisierenden Kennzeichen genügend klar ausgeprägt, um eine solche Unterscheidung deutlich zu machen? Die letztere Frage möchte ich mit ja beantworten und will ich nun Ihre Aufmerksamkeit auf die ihr am meisten ähnlichen Krankheiten lenken.

Im Anfang meiner Studien über dieselbe wurde in einigen Fällen ihre Ähnlichkeit in gewissen Entwickelungsstadien mit verwandten Affektionen aufgezeichnet; so finden wir z. B. in den Krankengeschichten von verschiedenen von mir referierten Fällen die provisorischen Diagnosen "Tinea circinata," "Ekzema," "Ekthyma," "Herpes," und "Pemphigus," und wurden diese Diagnosen nicht nur von mir selbst sondern auch von andern aufgestellt; einige der letzteren waren geneigt die vesikulösen und bullösen Varietäten als Herpesarten anzusehen und sie geradezu als Herpes gestationis, pyämicus, pruriginosus und Herpes circinatus bullosus zu bezeichnen. In anbetracht dieses Umstandes ist daher die Wichtigkeit einer Trennung der verschiedenen Varietäten der Krankheit, welche für sich bestehend so differente klinische Bilder zeigt, evident geworden.

Wer somit nur gelegentlich die Krankheit sieht, möchte wohl nicht leicht geneigt sein, die erythematöse und pustulöse Varietät auf einen und denselben Prozess zurückzuführen. Die erstere hat eine grössere Ähnlichkeit mit dem Erythema multiforme als mit irgend einer andren Hautaffektion und hat, wie ich in einem meiner Fälle festgestellt habe ('Medical Record, April 2nd, 1887) einige dieser Krankheit eigne Merkmale. Gewisse, gleiche herpetiforme Charaktere besitzen beide. Die Manifestation scheint in einigen Fällen

eine potenzierte Phase des Erythema multiforme mit chronischem Verlauf zu sein. In zwei Fällen, die mir erinnerlich sind, schienen ungewöhnliche Formen des Erythema multiforme zu gewissen Zeiten zu bestehen, aber als andre diesen unähnliche Eruptionsformen plötzlich auftraten, war diese Ansicht natürlich hinfällig. Der Umstand an sich, dass dieselben chronisch verliefen, widerstritt einer derartigen Auffassung. Es ist ganz bekannt, die Autoren verwerfen die Existenz eines Erythema chronicum multiforme, alle Schriftsteller nehmen nur einen akuten Prozess an und betrachten dasselbe als eine mit spontaner Heilung endende Affektion. So ist wenigstens z. Z. unsre Ansicht. Ich kann noch bemerken, dass die Effloreszenzen sich von denen des Erythema multiforme commune noch darin unterscheiden, dass sie weniger scharf begrenzt sind; sie sind weder hinsichtlich der Peripherie noch der Gestalt so deutlich markiert und bestehen mehr aus unbestimmt begrenzten Inflammationsherden als aus umschriebenen, scharf kontourierten Flecken.

Indem ich mich zum Herpes iris wende, welcher, wie allgemein anerkannt wird, dem Erythema multiforme am nächsten steht und überdies zuweilen nur ein vorgerücktes Stadium dieser Krankheit darstellt, halte ich es für unverkennbar, dass diese Affektion gleichfalls Merkmale mit Dermatitis herpetiformis gemein hat. Es muss indes bemerkt werden, dass in beiden von mir beobachteten Fällen schwerlich die Diagnose von Herpes iris von jemandem gestellt worden wäre. Der chronische Verlauf des Prozesses, wie er bei Erythema multiforme besteht, würde die Diagnose auf Herpes iris ausgeschlossen haben. Die Effloreszenzen sind dazu gar nicht von derselben Beschaffenheit wie die von Herpes iris; sie erscheinen von schlimmerem Charakter und werden von Hautstörungen intensiveren Grades begleitet, wie dies schon aus dem Charakter der Entzündung und der gewöhnlich vorhandenen Intensität der subjektiven Symptome hervorgeht, während die letzteren bei Herpes iris meist fehlen. Bei diesem ist die Eruption gewöhnlich auch lokalisiert, z. B. auf die Hände und Füsse. Universeller, über die gesamte Haut verbreiteter Herpes iris ist selten. Was das Erythema multiforme betrifft, so wird

es von den Autoren als eine benigne Affektion angesehen, die zwar stets einen akuten Verlauf zeigt, aber mit spontaner Heilung endigt, nur muss man des bekannten Umstandes eingedenk sein, dass sie Recidiven in verschiedenen Intervallen unterliegt.

Die bullöse Varietät kann Pemphigus vulgaris gleichen, wenn sie für sich allein besteht, und kann irrtümlich dafür gehalten werden. Wenn aber vesikulöse, vesiko-pustulöse und pustulöse Formen gleichzeitig vorhanden sind, ist ein Irrtum in der Diagnose kaum möglich.

Diese eigentümliche Mischung von verschiedenen Eruptionsformen findet bei Pemphigus nicht statt; wenn dann ferner bei dem weiteren Entwickelungsgang des Prozesses auf einen Schub Pemphigusblasen ein Ausbruch von herpetischen Pusteln und später Bläschen folgt, wird es dem Beobachter klar, dass er es hier mit echtem Pemphigus nicht zu thun hat. Eine derartige Entwickelungsgeschichte ist unvereinbar mit Pemphigus, der stets eine Blaseneruption darstellt, mag er akut oder chronisch verlaufen, einen ersten Ausbruch oder ein Recidiv bilden. Der Fall von N. B. E. (‘New York Med. Journ.,’ July 19th, 1884) mit der bullösen Form der Krankheit wurde zu verschiedenen Perioden seines Bestandes von den behandelnden Ärzten für Pemphigus gehalten, aber diese Ansicht auf Grund der nachträglichen Veränderungen und Entwickelung der Affektion bald wieder aufgegeben.

Verschiedene andre Krankheiten mit ähnlichen Kennzeichen wie bei unsrer hier erörterten Affektion können hier kurz erwähnt werden; so entwickeln sich gelegentlich bei Urticaria solche Symptome, und scheint diese Erkrankung ein Mittelding zwischen jener und Erythema multiforme zu sein, nichts destoweniger aber kennzeichnet der plötzliche Eintritt sowie der intensiv juckende Charakter der Efflo-reszenz die Urticaria. Eine bullöse Form von Urticaria dürfte wohl in keinem Stadium derselben vorkommen. In dem Fall von James W. (‘Phila. Med. Times,’ July 12th, 1884) fanden sich zur Zeit Pusteln, welche flach, ausgebreitet und serpiginös waren; hier war von einem Artze die Diagnose auf pustulöses Syphilid (Ekthymaform) zuerst gestellt und der Patient demnach einer antisyphilitischen Be-

handlung unterworfen worden. Solch ein grober Schnitzer dürft indes selten jemandem begegnen, welcher nur einige dermatologische Kenntnisse besitzt. Denn keine einzige Varietät deutet auch nur irgend wie auf Syphilis hin. Der eben erwähnte Fall hatte in einer späteren Periode auch einige Ähnlichkeit mit einem stärker entwickelten Stadium der Tinea circinata. Die kleinen stecknadelkopfgrossen, gelblichen, flachen Pusteln unmittelbar um die kreisförmigen und sich ausbreitenden Flecke herum liessen auf einen vegetabilischen Parasiten als Agens schliessen.

Es erübrigt nur noch gewisser Krankheitsnamen zu gedenken, wie im besondern der Hydroa einiger Autoren und der Hebraschen Impetigo herpetiformis. Diese Krankheitsformen können indessen nicht genügend erörtert werden ohne ein detailliertes Eingehen in dieselben, und erscheint es daher am besten hier sie gar nicht zu berühren.

Zum Schluss muss ich noch hinsichtlich des Namens Dermatitis herpetiformis und der Gründe für die Wahl dieser Bezeichnung ein Wort hinzufügen. Ein neuer Name war erforderlich und zwar ein solcher, der, ohne auf ein schon okkupiertes Terrain überzugreifen, am genauesten das Wesen der Sache ausdrückt. In anbetracht der ausgesprochen entzündlichen Natur des Prozesses war der Allgemeinbegriff Dermatitis einwursfsfrei. Auf Grund der Thatsache, dass Polymorphie während des ganzen Krankheitsverlaufes ein hervorstechendes Zeichen war, hielt ich im Beginn meiner diesbezüglichen Studien die Bezeichnung polymorph oder multiform für passend; dieser Begriff schien mir ausserdem weit genug, um gegebenen Falles eine lange Reihe von mehr oder weniger ähnlichen Exanthemen in sich zu schleissen. Aber in Hinsicht darauf, dass unsre Nomenklatur bereits eine gut definierte und allgemein anerkannte Dermatitis von verschiedener Art mit einem sehr ähnlichen Titel, nämlich Erythema multiforme, enthielt, schien mir genügend Grund vorhanden, mich nach einem andren umzusehen. Verwirrung, ja selbst der Schein einen solchen, musste vor allem vermiden werden. Dermatitis multiformis hätte man leicht und natürlicherweise für ein vorgerücktes Stadium von Erythema multiforme ansehen können. Es war deshalb eine andre und präzisere Bezeichnung wünschenswert; diese

schien mir in dem Wort herpetiformis zu liegen, zumal dieser Terminus bereits mit einer verwandten Krankheit, der von Hebra beschriebenen Impetigo herpetiformis verbunden war. Herpetiform bezeichnete überdies das am meisten charakteristische Merkmal des pathologischen Prozesses. Es wurde als ein wesentliches angesehen, ohne welches die Krankheit überhaupt nicht existierte, und deshalb war herpetiform passender als multiform, welch letztere Bezeichnung nur auf das klinische Gepräge der Krankheit sich beziehen konnte. Dieser ihr originaliter verliehene Name scheint mir ganz passend und kann auch vorläufig beibehalten werden, bis unsre Kenntnis der Krankheit vollständiger als jetzt ist.

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## CASE OF DERMATITIS HERPETIFORMIS

### CAUSED BY NERVOUS SHOCK.[1]

In November, 1878, I was asked by my friend the late Dr. F. F. Maury to see a "curious case of bullous skin disease" under his care. It proved to be a marked example of what I have described as dermatitis herpetiformis.[2] The following notes, which I think worthy of record, were made at the time. The disease was then fully expressed, and showed the lesions not only in abundance but in all stages of development.

The patient (Capt. K—) is a man thirty-four years of age, of large frame, stout and strong, and in the enjoyment

[1] Reprinted from the 'American Journal of the Medical Sciences' for January, 1885.

[2] Communication read before the Section on Medicine of the American Medical Association, May 6th, 1884, 'Journal of the Am. Med. Assoc., Aug. 30th, 1884; see also 'Amer. Journ. of Med. Sci.,' Oct., 1884.

of good general health. He never experienced any disease of the skin until six weeks ago, when the present eruption made its appearance. There is no family history worthy of record.

While gunning in the meadows he unexpectedly found himself in a bog of soft, blackish, strong-smelling earth, into which he sank deeper with every step. He at once recognised the nature of the spot and the danger, and endeavoured to extricate himself, but this proved no easy matter, for with every step he sank deeper into the mire, until in a short time he was buried up to his armpits. He realised his extreme danger, and looked forward to a speedy and miserable death. After struggling for a full half-hour in the above predicament he succeeded in seizing a tuft of grass just within reach. By gradually working himself loose and pulling on the grass he finally, in an exhausted state, managed to reach firm ground. He was carried home in a weak condition, bathed and cared for. Three days after this adventure, which had greatly shocked his whole system, the eruption appeared in the form of small, variously shaped, round, oval, and angular vesicles, or small "blisters containing clear fluid."

They came out in number, and were scattered over the flexor surfaces of arms and forearms. When first noticed they were pin-head in size, and were not accompanied by areolæ, but seemed to rise directly from the sound skin; two days later, however, inflammation surrounded their bases. At first they were free of itching, but towards the fourth or fifth day, by which time they had slowly grown to the size of peas, this symptom set in violently. On the second day of the attack scattered lesions of the same character appeared here and there over the trunk, legs, and thighs, and were especially numerous on the posterior surfaces of the thighs, over the shins, and about the ankles, and were quite symmetrically distributed. On the trunk they were on the back, chiefly between the scapulæ, and on the abdomen about the umbilicus and pubes. On the chest they were few in number and disseminated.

By the fifth or sixth day they had attained the size of large peas—in short, became *blebs*; were tensely distended

with clear, serous contents; showed no disposition to rupture; and were accompanied with slight areolæ. The itching now became annoying and was constant, the desire to scratch being uncontrollable. The general health remained good; no chilliness or fever. About this date he was rubbed with olive oil, which aggravated his condition, the skin by the next day becoming hot and more irritable. New lesions continued to appear, especially on the back, and the older ones increased in size without showing any sign of rupturing, and where two or more were in close proximity they often coalesced.

From the sixth to the thirteenth day he had no rest, the itching being of the most harassing character. About the eleventh day the lesions became darker, the contents showing a distinct orange-yellow colour, and instead of being serous in character were thicker and of a "jelly-like" consistence, so that when the blebs opened with a knife the mass could be removed as a semi-solid gelatinous substance. On the fourteenth day the skin generally and the lesions assumed a dark reddish, bluish-red colour, while the latter contracted and in a few days became crusted and hard, so that with his finger he could "knock them off," a dark reddish stain remaining. The eruption at this date was at its height. The blebs were very numerous, the whole surface being literally covered. The scalp, face, ears, penis, and scrotum, and even the verge of the anus, were attacked, the palms and soles being the only regions that escaped. The mouth was likewise unaffected. The lesions varied in size from a pea to a walnut, the average size being that of a silver dime; the larger ones were generally formed by the coalition of two or more lesions. They were semi-globular in shape, tensely distended, and in no instance flattened or umbilicated. None burst spontaneously, but many were ruptured by violence; they invariably burst with a "crack" or "explosion." As already stated, crusting took place in the course of a few days, the crust being of a yellowish-brown or dark brown colour, and not bulky. After these became detached, he observed about the bases of the original lesions a few small pin-head sized "whitish points" or pustules, which multiplied and grew rapidly, itched, and burned; were

raised; ran together in many instances; and in four or five days developed into large yellowish *pustules*, some of them being as large as cherries. Nearly all of these lesions, hundreds in number, were punctured, the walls collapsing and the contents flowing freely, but being somewhat turbid. This outbreak constitutes what he terms the second attack. The lesions were as abundant as in the first attack, and while showing a disposition to appear on the sites of the old lesions yet came out also on sound skin. Poultices were applied, and later crusts formed as before, which in the course of a few days became detached, leaving dark reddish spots and stains.

He now rapidly recovered and remained nearly well for a week, when the third attack set in. This was ushered in by malaise, chills, heat, nervousness, and a general itching of the surface, the eruption developing much more rapidly than before. The lesions were for the most part distinctly *pustular* in character, the others being *vesico-pustular*, *vesicular*, and *bullous*; were flat, surrounded with inflammatory areolæ, and itchy. They appeared only on the extremities and over the abdomen. They differed in their distribution from the former lesions in being *grouped*, two, three, or more manifesting themselves in close proximity, often coalescing.

*Present Condition.*—November 22nd, 1878. He is now suffering with the remains of the third attack, just described, to which within the week has been added a fourth outbreak. New lesions have been coming out from day to day. He is confined to bed, and is suffering with a profuse multiform eruption occupying the greater portion of the general surface. It consists of *vesicles*, *blebs*, *vesico-pustules*, and *pustules* of various sizes and shapes, and in all stages of evolution; *erythematous* (light and dark red) *patches* and *stains*, for the most part the remains of former lesions; *excoriations* and *scratch-marks*, and *crusts*, though these latter lesions are by no means abundant. The multiformity of the lesions is striking. Vesicles, blebs, and pustules are in about equal proportion, and are so intermingled as to exist side by side. The vesicles and blebs may be first considered, and I speak of together, them for it is impossible to draw a line

of distinction between them; the difference is merely of size. They exist in large numbers, in hundreds. They vary in size from a pin-head to a walnut and larger, the majority averaging between a split pea and a hazel-nut. They are semi-globular or flat in form, and are either tensely distended or flaccid, the former condition existing in all of the smaller lesions. They rise abruptly from the surrounding skin to the height of from one to several lines, have moderately thick walls, similar to the lesions of pemphigus, and show no disposition to rupture spontaneously. There is no sign of umbilication. They are of all shapes, the majority being circular or ovalish; but some are irregular in outline and show angular, "puckered" borders, as is often seen in herpes zoster, in which event they are usually surrounded with bright red, highly inflammatory areolæ. Many of the vesicles and blebs rise up without areolæ, looking like magnified sudamina. They have a pearly or pale yellowish colour, and, as in the case of other similar lesions, refract light, which gives them a glistening appearance. The contents are for the most part clear, but some are cloudy, and in many instances are more or less tinged with blood, producing a mottled or streaked bluish-red hæmorrhagic look.

The pustules are likewise in all stages of evolution both as to size and extent of pustulation. Some are distinct pustules no larger than pin-heads, flat or semi-globular in form, and circular or irregular in outline; while others of the same size and larger have evidently been vesicles and blebs, and are passing into pustules. Still others are the size of peas and cherries, and are distinctly pustular, like the lesions of true simple impetigo, and contain whitish, pale yellowish puriform contents. Some are in a perfect state of preservation, semi-globular or acuminate in form; others are more or less collapsed. As stated, inflammatory areolæ surround almost all of the larger pustules.

As regards distribution, no region is free except the palms of the hands. It is a very general eruption, the lower extremities exhibiting the most lesions. The flexor surfaces are especially invaded. Upon the thighs and legs there is not a square inch that is not the seat of disease. The skin which is not occupied by distinct lesions is dark red and

violaceous in colour. The ankles are literally encircled with blebs and pustules, many of which have run together, forming large, elongated, flaccid, partly bloody, dependent blebs. There is everywhere a tendency for the lesions to group, and while owing to their great multitude this is not striking in all regions, it is nevertheless very manifest in certain localities, as on the buttocks and thighs. The groups are for the most part small, consisting of from three to five lesions situated within a radius of an inch. In other places a dozen or more lesions occupy an area the size of the palm of the hand.

A peculiarity of the lesions is their disposition to coalesce. Inclining to manifest themselves in ill-defined clusters of two, three, or more, as they increase in size they run together, forming larger lesions. Around the immediate circumference of these lesions, whether vesicular or pustular, smaller flat pustules or vesicles, the size of pin-heads, are in many instances present. When ruptured the lesions crust over with flat, light yellowish crusts. Removing these, superficially excoriated, moist, reddish surfaces, having sharply defined irregular vesicular or pustular borders, are exposed to view. Everywhere about the older lesions there is noted a disposition on the part of the process to extend itself in a creeping manner while healing in the centre. Itching is present, and is very distressing.

December 19th.—A month has elapsed since the last note. During this period four distinct attacks or crops of eruption have manifested themselves. The lesions in the first three attacks were of the same character as those in the outbreak of November 22nd, just described at length, namely, vesicles, blebs, and pustules, with but little inclination to intermediate forms, while in the present eruption *vesico-pustules* predominate. The last two attacks have been milder, with smaller lesions, but accompanied with more itching. The general course of the disease, the disposition of the lesions to cluster, and the regions invaded, have been the same as on previous occasions. At present the eruption is characterised by many small, and some large, variously shaped *vesicles*, *vesico-pustules*, and *pustules*, occurring in patches or scattered over the surface, in all stages of evolution, together with

numerous excoriations, ruptured or torn lesions, crusts and scales seated upon a dark red, violaceous, mottled, pigmented skin, the remains of former attacks. The patient is able to be about the house; his general health is good. He has used lately alkaline tarry lotions. Arsenious acid, in doses of one-fortieth of a grain, has also been taken for the last three weeks; also quinia, and a general tonic treatment.

In December, 1882 (four years after the last note), I received a note from the patient, stating "I am still troubled with the disease, and it has not failed to put in an appearance at certain periods since you saw me in 1878, although the blisters and pustules have gradually become less, both in number and in size. At certain times since, within the year, I was so free of eruption that at one time I thought surely I was rid of my pest. I can always tell two or three days before the eruption will appear by the coming on of an itching sensation. During the past six months I have had two attacks."

The history of this case, including the cause of the disease—a violent shock to the nervous system—is both interesting and instructive. The bullous variety predominated, and when I first saw him, it was highly developed; subsequently, however, (as in almost every case that I have encountered), other lesions, especially pustules, manifested themselves. The constitutional symptoms accompanying one exacerbation were marked.

## ON THE RELATION

OF

# IMPETIGO HERPETIFORMIS (HEBRA AND KAPOSI) TO DERMATITIS HERPETIFORMIS (DUHRING).[1]

As there have been considerable discussion and some diversity of opinion as to the propriety of grouping impetigo herpetiformis under dermatitis herpetiformis, I desire briefly to present my reasons for having originally adopted this view. It may be well to premise my remarks with the statement that heretofore, in my several communications on this disease, I have confined my observations largely, if not exclusively, to the cutaneous manifestation—to the skin disease proper—with the idea mainly of calling attention to the multiform phases of the disease. The symptoms alone, it may be said, have up to the present time received attention; the equally if not more important subjects of etiology and pathology being for the time intentionally slighted. In all rare or obscure affections the eruption itself, including its history, symptoms, evolution, and involution, is first to be considered. After these points have been determined upon, as far as the material at hand will permit of, the questions of the cause and nature of the disease naturally follow for investigation and discussion. In addition to the clinical memoranda and observations presented from time to time, I have sought to bring together into one group such previously reported cases, scattered throughout literature, and certain other allied forms of disease, as seemed to me might properly be included under one head. Circumstances have, for some time past, prevented me from continuing my

[1] Reprinted from the 'American Journal of the Medical Sciences' for March, 1890.

study on the subject, which will account for what may seem indifference or neglect of the question.

It is now over five years since I first called attention to a disease of the skin which, up to that time, had not received special notice. A number of cases of a peculiar cutaneous disease had, from time to time, previously come under my observation, all possessing certain striking features in common when viewed in their totality—that is, throughout their complete history, including relapses. There existed manifestly several quite different varieties of the affection, as shown by the presence in some instances of a decided predominance of certain lesions, while in other cases different forms even prevailed. But beneath this cloak of multiformity, and notwithstanding the occurrence of diverse lesions simultaneously or of those which made their appearance from time to time as the affection ran its course, certain striking pathognomonic symptoms could not fail to impress themselves upon the observer, showing the existence of a peculiar and undescribed disease. Had a few cases only been encountered at long intervals, these features might not have been recognised so readily.

As the disease represented by these examples was practically unknown and had no place in literature, it seemed necessary to bestow upon it a title. The relatively large number of cases that I had encountered seemed to warrant such recognition. By reason of the uncertain and variable character of the eruption, of its conspicuously diverse primary lesions and their distribution and arrangement, occurring in the several forms or varieties in which it usually appeared, and, moreover, because of its distinctly herpetiform feature, the name dermatitis herpetiformis was selected. The term dermatitis, owing to the idea of wide-spread or general and varied inflammation thereby conveyed or implied, and because of its being non-committal as to etiology and pathology, appeared to meet the requirements better than any other that suggested itself; while one of the most distinctive characteristics was made plain by the word herpetiform. To this latter point I wish to direct special attention, and I would here say that the herpetiform element has been present in all of the cases (now, perhaps, twenty in number)

that I have seen, in some instances marked, in others existing to a moderate or only a slight extent.

As the matter stands to-day, the disease is sufficiently well defined to be readily recognisable by all observers where typical cases are concerned. I cannot well see how pronounced forms, especially if held under observation long enough to note the ever-changing lesions and the varied aspect of the eruption, can be confounded with other better known affections. In ill-defined, atypical forms it is, of course, liable to be mistaken for certain other diseases to which it may bear more or less resemblance, more especially erythema multiforme, herpes iris, pemphigus, and eczema, according to the views held by the observer, precisely as in other doubtful forms of skin disease. Thus, for example, as is well known, discrepancy in diagnosis is not infrequently encountered in eruptions characterised by the formation of blebs, one observer regarding all such manifestations as varieties of "pemphigus," another merely as instances of "bullous disease,"—a vague, non-committal expression, plainly indicating an unwillingness on the part of the observer to subscribe to the view that every bullous eruption must necessarily be pemphigus.

The relations of dermatitis herpetiformis to erythema multiforme, herpes iris, and pemphigus are, I need not say, most interesting and important topics, to which I naturally have had my attention directed. But these subjects cannot be entered upon without a great deal of discussion. Here, at once, arises the matter of definition. For example, how shall these diseases—erythema multiforme, herpes iris, and pemphigus—be defined? What forms of eruption shall be included and what excluded under these names? Shall the old, time-honoured, classic definitions continue to be observed, or should new ones be framed to take in enlarged views concerning these processes? This question cannot be entered into at present, nor do I wish now to speak of the relation of dermatitis herpetiformis to the diseases just cited, nor to any other vesicular, bullous, or pustular affections, except one, namely, the impetigo herpetiformis of Hebra.

At this point I must be permitted to go back a few

years, in order to make my position, views, and reasons therefor clear. As is known to all, Hebra described, in 1872, a grave pustular disease of the skin, of which several instances had, from time to time, been observed at the Vienna General Hospital. The description given was brief, and in the dermatological world at large the subject attracted comparatively little attention. Dermatologists in other parts of Europe and in this country seemed at a loss to identify or recognise the disease. In the United States it did not seem to be known. My American fellow-dermatologists in the large cities, with whom I conversed, were not familiar with it, nor was I myself able to reconcile Hebra's description with any of the pustular affections encountered in my field of study. Nor was the disease recognised either in France or England. Moreover considerable confusion existed even in Vienna, competent observers there being by no means of the same opinion regarding the disease and its proper classification. Thus Hebra himself first looked upon it as belonging to the herpes group, and called it "herpes impetiginiformis," with the idea that it was a form of herpes; subsequently he regarded it as an herpetiform impetigo. Nor was the subject materially elucidated by the publication of several of Hebra's original cases by Auspitz and by Geber, the first of whom looked upon it as herpes, calling it "herpes vegetans," while the latter also endeavored to prove it to be herpes. Then Neumann, who was without doubt familiar with Hebra's cases, emphatically designated it herpes, terming it "herpes pyæmicus" or "herpes puerperalis." Even at this later date, notwithstanding all that had been written by the Viennese dermatologists, the subject was far from clear to the minds of foreign dermatologists. The consensus of opinion on the part of the Vienna observers, however, seemed to be that the disease was an undescribed form of herpes, as is evidenced by the names decided upon by the several reporters. Nor, finally, was the matter made plainer by Hebra himself, who stated that the case previously reported by himself and Baerensprung as "herpes circinatus," and figured in their atlas of skin diseases, was also an example of this same disease, namely,

impetigo herpetiformis. It need scarcely be said now, in passing, that if the views (to be referred to) recently put forth by Kaposi be accepted, this peculiar case must be excluded from the list. No further examples were at this period reported, and the matter for the time being remained quiescent.

In the meantime, in Philadelphia, during this epoch (from 1870 to 1880), a series of cases of an unknown, inflammatory, polymorphous affection of the skin had come under my observation—some in hospital, others in private practice. Among these was one which, when it first was brought to notice, appeared to me (and to other physicians who saw it) to be an example of the impetigo herpetiformis of Hebra. It apparently represented a mild expression of that disease, and showed the chief clinical features depicted in one of the portraits (case of 1871) in Hebra's atlas. The resemblance was striking. The cutaneous manifestation was altogether novel, and I was unable to classify it elsewhere.

The patient was a woman. The eruption was general and extensive, and was exclusively pustular (with no signs of erythematous, urticarial, vesicular, or bullous lesions) and crusted, the pustules being whitish and yellowish, and of varied shapes and sizes, some being distinctly elevated and somewhat conical or rounded, others flat; some were miliary, others small, pea-sized, and some larger; all being seated on more or less inflamed bases or arising from inflamed patches. The eruption, as a whole, was, moreover, herpetiform, showing a distribution and arrangement *here and there* similar to that seen in imperfectly developed or abortive herpes zoster. The lesions themselves were *irregularly* grouped, as is sometimes noted in small discrete patches of zoster. The central pustules, often aggregated in little bunches of two, three, or four, were small but of variable size; the older ones were more or less crusted, and were closely encircled in an incomplete, broken manner, with new, for the most part sparse, flat, minute pin-head sized pustules. There was, moreover, marked pigmentation in patches here and there; also malaise, with a disposition to be cold and hot alternately, hardly amounting to a regular

chill. Finally, there were heat and burning and some itching, but recent scratch-marks were not conspicuously present. In brief, the case possessed, so far as the skin was concerned, the chief characteristics of Hebra's impetigo herpetiformis, and this diagnosis was accordingly made. The disease persisted, the eruption repeating itself in a succession of crops with the same kind of lesions, and within six months disappeared, to be replaced, however, by an altogether different dermatological picture,—one with which I was quite familiar, namely, a polymorphous, mixed vesicular and bullous, inflammatory, herpetiform eruption, accompanied with severe burning and itching, or, briefly, the typical form of dermatitis herpetiformis. Subsequently the previous impetiginous or strictly pustular form recurred, manifesting itself precisely as before ; and during the next year the eruption again became vesicular and bullous.

There was now, after several years of observation, but one conclusion to draw—namely, that these diverse cutaneous manifestations all belonged to one pathological state, were simply varieties, or forms, of one process. Other similar cases later came under notice which strengthened this view, and I accordingly expressed myself that Hebra's impetigo herpetiformis (as I understood that disease from Hebra's description and portraits) might be regarded as a pustular manifestation of an extensive multiform (erythematous, vesicular, bullous, and pustular) herpetiform disease of the skin. This view, moreover, seemed to be supported by a case of "impetigo herpetiformis and pemphigus" reported by Heitzmann, of New York, which, while it presented the characteristic cutaneous features of Hebra's disease for a period of several months, abruptly changed from a pustular to a bullous affection, the blebs being in all respects like those of pemphigus. From this case Heitzmann drew the conclusion that both diseases arose from identical causes, and should be considered as being kindred to each other. It may be added that in this case the disease did not occur in connection with pregnancy, and that no cause could be assigned for its presence, the patient having been an apparently healthy woman, fifty-two years of age. The disease, nevertheless, ran a fatal course in about eight months from the beginning, œdema

of the meninges setting in toward the end. There can scarcely be any question here concerning the diagnosis of impetigo herpetiformis, for Dr. Heitzmann had not only seen three of Hebra's cases in Vienna, but had, moreover, painted the portraits which portray this disease in Hebra's atlas.

The subject remained *in statu quo* until my several communications appeared, and, later, Kaposi's valuable contribution on impetigo herpetiformis in 1887, in which the relations of that disease to some other affections (including dermatitis herpetiformis) are discussed. From this latter article a much more satisfactory idea of this disease is obtained than from any previous publication. The subject is presented in a different if not a new light, and is fortified by reference to additional and more recent observations, and we are enabled to note what the author would have us regard as impetigo herpetiformis. If this definition, then, is to be accepted, and to be restricted so as to include only such cases as the author refers to, I admit that it becomes questionable whether the disease should be regarded as a variety of dermatitis herpetiformis. If the definition is to be rigidly confined to such cases (including their nature) as Kaposi quotes, the disposition of the matter would be simple; but other observers of this disease (or what they assume to be the same affection) do not entirely agree with the Vienna dermatologist. According to Kaposi, *the disease is invariably characterised by superficial miliary pustules, which begin as such and remain unchanged throughout their entire course, always arranged in groups and clusters, new lesions appearing on the border of older and crusted confluent pustules, in one or more series, on inflamed bases, while recovery takes place in the centre; furthermore the disease occurs only in pregnant or puerperal women, and is accompanied with chills and marked fever, and is almost invariably fatal.* This definition is clear and simple enough, but does it include all forms of the disease? Is it sufficiently comprehensive? The question might pertinently be raised, is it wise to make the definition so circumscribed; is the disease not liable to vary from this type; does it invariably show these very precise features; are, for example, the pustules always

miliary, and from beginning to end; may they not vary in size, and, more especially, be considerably larger? Surely one portrait of this disease in Hebra's atlas (case of 1871, referred to before) fails to portray a miliary eruption; on the contrary, not only are many of the pustules large, but there is, moreover, considerable variation in size; nor is their arrangement and mode of extension or spreading apparently like that depicted in the other cases, namely, peripherally, as in herpes circinatus. I may remark further on this point that I find it difficult to reconcile this portrait with Kaposi's description of the eruption, and, finally, that it was mainly upon this illustration that I ventured to base the opinion of the identity of one of my cases (that of Annie McC—, 'Journ. of Cut. and Ven. Dis.,' vol. ii, No. 8) with the disease depicted. If Kaposi's views be adopted, Heitzmann's case, already referred to, cannot be regarded as impetigo herpetiformis, although, as previously remarked, from the fact that Heitzmann had the opportunity of seeing several of Hebra's original cases, it would seem that he must be entirely familiar with the subject. Nor can Zeisler's case ('Monatshefte für prakt. Dermat.,' 1887, No. 21) of so-called "impetigo herpetiformis," which he, Dr. Hyde, and others believed to be an example of the Hebra and Kaposi disease, be regarded as such.

It may be questioned further, Does impetigo herpetiformis in all instances exhibit the same grave general symptoms and course, terminating in almost every case fatally? Such symptoms and termination assuredly might be anticipated if it were generally admitted that the cause was uniformly septicæmia,—that the disease was always of septicæmic origin. But may not various causes give rise to the same cutaneous manifestations, not only here, but elsewhere, as in the case of certain other affections of the skin—as, for example, eczema? There was a time, not long ago, when Kaposi held that the disease occurred exclusively in women, but lately he has himself given the notes of a case observed in a man. From this criticism I wish merely to intimate or suggest that our definitions should not be drawn too closely. Most observers will agree that as our experience enlarges in dermatology we find in all directions the need of

more breadth or latitude. Expansion in almost all instances, we note, comes sooner or later.

I have thus endeavoured to present a concise historical sketch of impetigo herpetiformis, and also, more particularly, to state my reasons for having, in my earlier papers, regarded it as one of the manifestations of a peculiar, polymorphous, extensive process designated dermatitis herpetiformis. Whether I was right or in error in advancing this view is a question depending largely, in my opinion, upon the definition that shall be accorded to impetigo herpetiformis; and here I may remark that it is far from my thoughts to undervalue the observations of the distinguished Vienna dermatologist, whose extended and unique experience with impetigo herpetiformis entitles his communication to due consideration. My desire has been from the beginning simply to arrive at the true position which that disease occupies, and more especially to define its relationship to other allied affections. I may say, in passing, that had Kaposi's article been published at the date of my several communications, I should probably have, in some degree, qualified the conclusions concerning the identity of the affections.

In bringing these remarks to an end, I would say that I have always held to the opinion that all discussions tending to create perplexity should be avoided. On this point I feel strongly in the present case concerning the relationship of the two forms of eruption which are the subject of this paper. The matter can only be settled by fully recorded observations at the hands of competent reporters, and it is highly important for future studies and deductions that the cases be ranged under such titles as will convey the clearest idea of the clinical picture. Considering, therefore, the existing difference of views, and in order that no possible barrier may impede progress, it will perhaps be to the advancement of the subject to separate, for the present at least, the diseases; and that, in the future, observations be reported under one caption or the other, as may seem most in harmony with the clinical facts of the case.

# CASE OF TYPICAL DERMATITIS HERPETIFORMIS.[1]

During the past month a typical example of this affection has been under almost daily observation, and the symptoms have been so pronounced and so characteristic of the usual form of the disease that I desire to add the case to the list of those already published. I describe the case, moreover, because there seemed to be some doubt as to the diagnosis in the minds of the several well-known practitioners who had charge of the gentleman before he came under my observation.

Mr. S—, of Cincinnati, consulted me about the middle of January of the present year, with a letter describing his previous condition and treatment from Dr. Ransohoff, under whose care he had been for some time. The doctor's letter states that the patient (a man about fifty years of age and of dark complexion), who had before always enjoyed good health, manifested "squamous eczema" of both hands about a year ago. Four months later the present illness began with the development of blisters of the size of a pea or bean on the hands, wrists, feet, and ankles. In July last a fully developed "pemphigus simplex" existed, the blebs being as large as a silver dollar, tense, and containing a clear fluid. These appeared in successive crops all over the body. During the four months of the acute attack hardly a square inch of the surface was left uninvaded. When the blebs disappeared excoriations of similar dimensions remained, but which were soon covered again with epidermis.

Loss in weight, most distressing itching ("pemphigus

[1] Reprinted from the 'American Journal of the Medical Sciences' for June, 1890.

pruriginosus"), and from time to time septic manifestations; low, muttering delirium, slight elevation of temperature, rapid and irregular heart action, heavily coated, dry tongue, diarrhœa, and profuse night-sweats were all present. Under sustaining treatment and local remedies, such as the continuous bath for two weeks, swathing in oil, oxide of zinc and bismuth bandages, the patient finally began to improve, and was able to leave home for a change of climate. When last seen the itching still persisted, and the skin, especially of the extremities, presented a livid hue and was sodden. It, moreover, was elevated in the form of large indurated papules where formerly vesicles (which did not rupture) had existed. Dr. Ransohoff concludes his letter by stating that at first the diagnosis of dermatitis herpetiformis was made, but that later, when at its height, the disease seemed to possess the features of pemphigus pruriginosus; while still later, as improvement set in, it again approached dermatitis herpetiformis.

When I first saw the case the skin was much inflamed, excessively pigmented, of a dirty-looking, mottled, yellowish-brownish colour, thickened, and the seat of an extensive eruption, consisting of small and large, more or less confluent, inflammatory patches, together with distinct individual lesions, occupying almost the entire general surface. The trunk and the upper and lower extremities were completely covered with a multiform eruption of a mixed chronic, subacute, and acute character, arising from a chronically inflamed, infiltrated, and toughened skin. The greatest possible variety of inflammation existed in the form of a continuous mass or sheet of eruption, there being no healthy skin on the affected regions.

The lesions were macules, maculo-papules, papules, irregularly shaped and defined, flat or spread out (as in erythema multiforme), and of variable dimensions; vesico-papules and vesicles varying in size from a small pin-head to a pea, some being flat, glistening, and blister-like, others raised and surrounded with a somewhat drawn together or puckered, highly inflamed base, as in herpes zoster. Many of the vesicles were minute and scarcely visible, except in oblique light. Here and there blebs existed, some small,

ers large; also small pustules, which evidently had begun pustules, some of them being flat and punctate, pin-head l millet-seed sized.

On the shoulders and upper part of the back the existe of small, mostly miliary lesions (papules, papulo-vesicles, l pustules), commingled and in all stages of evolution, d grouped into patches, some of them marginate, together th the marked pigmentation, suggested a likeness to a acute, copious, miliary, herpetiform syphiloderm.

Excoriations and abrasions due to scratchings, blood-sts, and slight yellowish and brownish crusts about the nmits of vesicles and pustules, together with torn adrent epidermis, were also present, the whole picture being e of great multiformity, such as is noted in no other ease. As is well known, marked multiformity is often served in scabies of several months' duration, but the ection here was even more polymorphous than occurs in t disease.

The lesions were aggregated, grouped, and disseminated, t the eruption, as a whole, was herpetiform—the distribun, general arrangement of the individual lesions and of e patches, the progress and the manner of extension, all ggesting certain symptoms common to erythema multi-me, herpes iris, or herpes simplex. Here and there the se grouping or bunching of three or four usually minute small vesicles or vesico-pustules upon an inflamed base sembled an abortive patch of herpes zoster. The disease, wever, bore more likeness to erythema multiforme of an vanced stage and of a severe type than to any other affecn. Furthermore, itching and burning were present to an cessive degree, tormenting him by day and by night. He s, moreover, nervous, irritable, and anxious.

I will now enumerate the local remedies that were emyed, and comment briefly on their action, which, it may here remarked, was far from satisfactory.

The patient stated that a number of remedies had been eviously used without affording much relief, among them e various soothing and more stimulating washes and ointnts useful in eczema. Those prescribed by me consisted sulphur in the form of ointment, both weak and strong,

and also in the form of a dusting powder, liquor carbonis detergens, ichthyol, as a wash and as an ointment, weak and strong; mild salicylic acid ointment, fluid extract of grindelia robusta as a lotion, weak and strong, and carbolic acid as a lotion, all having been made use of from time to time. The most useful were sulphur ointment, two to three drachms to the ounce, and liquor carbonis detergens, from one half to two drachms to the ounce. These remedies, as well as others, were employed on various parts of the body, and with each experiment it was the rule to make the application of one remedy to one lateral half, and another to the other half of the body, with the view of determining the relative merits of each. The fluid extract of grindelia robusta on several occasions was found to be of some value, but the sulphur ointment was the most useful. This was used with considerable friction in order to break down the vesicles, as in the case of scabies, and on several occasions improved the skin and relieved the itching. Internally, antipyrin, antifebrin, phenacetin, chloral, and belladonna were all prescribed to meet symptoms, but with only moderate success.

During the four or five weeks which followed, the disease on two occasions improved considerably, but again became worse, the process manifesting itself in the form of exacerbations, each lasting about a week. Now and then large blebs formed here and there, especially on the thighs. On the trunk the lesions were at one time more erythematous, at another time more vesicular. The herpetiform element, more or less well-defined, remained constant, and constituted a feature of the disease.

In conclusion, the case may be summed up as showing the disease in its typical form, characterised by a multiform eruption of slightly raised, erythematous, herpetic patches, more or less confluent, together with papulo-vesicles and vesicles and blebs of variable size, shape, and outline, likewise, as a rule, herpetic. The thickening of the integument and the marked pigmentation from the oft-repeated attacks of eruption and scratching, and the itching and burning were also conspicuous symptoms. The general health was at times considerably disturbed, as shown by the nervous,

anxious, irritable state, the loss of appetite and of sleep, and the excessive sweating and great thirst. The urine was cloudy and dark, and variable in quantity, as is the case in other forms of general nerve depression.

In the matter of diagnosis, the disease, during the period it was under my observation, could hardly be mistaken for any other affection; surely not pemphigus, because blebs were the exception; nor would eczema suggest itself, because of the prevailing herpetiform characters of the individual lesions and of the patches. Everywhere and on all occasions the eruption showed itself to be under the control of the peripheral nerves, as in the other more marked and better known forms of herpetic diseases.

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## THE TREATMENT OF DERMATITIS HERPETIFORMIS.[1]

In the several communications on this disease that have been published by me during the past five years, no special remarks have been made concerning its treatment. The subject-matter of these papers has been largely confined to a statement of the cases observed with the view of setting forth the symptoms and the more important clinical facts, in the hope that the disease might become better known. A number of cases (perhaps ten or twelve) have been reported by me, and others have been observed in my private and public practice, so that now it seems appropriate that something should be said about the treatment of this exceedingly rebellious disease. At the same time, I would state here that in many cases the remedies employed, both external and internal, seemed to exert but little or no bene-

[1] Read before the American Dermatological Association, September 3rd, 1890. Reprinted from the 'American Journal of the Medical Sciences' for February, 1891.

ficial effect. In severe cases, and especially during an exacerbation, no form of local treatment used appeared capable of making a favourable impression on the skin. In such instances the disease is the most difficult to influence of all the inflammatory affections, surpassing even inveterate eczema.

The internal treatment may first receive attention. The generally-recognised observation that the disease may arise from and be dependent upon several distinct or even diverse causes—precisely, for example, as occurs in the case of eczema—precludes positive statements as to remedies. Each group of cases, based on the etiological factors at work, requires special handling, and hence I believe no class of remedies can be recommended which would be suitable to all cases. The origin of the disease, where this is ascertainable, should ever be kept in mind, and the treatment be pursued in this direction on general principles. With a disease which in most instances is exceedingly persistent and chronic in its course, a speedy cure is not to be looked for, either from internal or local remedies.

I shall make my remarks as practical as possible and be brief. The local treatment may first be considered. It must be remembered that the disease, as a rule, is multiform in character, and that, as in the case of eczema, we have to deal with varied lesions, at one time erythema, at another vesiculation or pustulation. The several varieties of the disease, therefore, naturally call for different formulæ, certainly as to strength, and sometimes even for different remedies. Thus, my experience has shown that milder preparations are required for the erythematous than for either the vesicular or bullous, and I would here remark that this (erythematous) variety is the most difficult of all to control by local means, while the vesicular is the most easily influenced. It is not my purpose at present to take up the treatment of the several varieties of the disease specially, but rather to ask attention to the principles of treatment applicable to the disease as a whole. From a therapeutic standpoint the affection may be considered under the headings of acute, subacute, and chronic, the two latter stages being those we are generally called upon to treat. It

must be kept in mind that the disease involves in most cases the greater part of the general surface; that therefore there is a good deal of cutaneous surface requiring attention, and that the remedies must be selected and prepared to meet that end. Another difficulty that we have to contend with is that the eruption tends to repeat itself in the form of more or less frequently recurring outbreaks or crops, a new one often coming out before the old one has disappeared, the skin thus being in a peculiar state, interfering with and complicating the treatment. It is this condition and the variety of elementary and secondary lesions generally present at the same time that render the treatment so difficult. Almost all the cases that have been under my observation have been chronic, and previously had undergone all manner of treatment; in some instances at the hands of competent dermatologists. Long experience has taught me that the disease is most difficult to control, and that some of the remedies from which good results might be looked for—such, for example, as are useful in eczema—exert but little or no influence in arresting the process. The milder so-called soothing preparations, as boric acid, calamine and oxide of zinc lotions, ointments, and pastes, sometimes so useful in acute or subacute erythematous and vesicular eczema, are of no value in this disease. I have long since arrived at the conclusion that the only class of remedies from which benefit is to be expected is stimulants, especially those which act revulsively. I will first enumerate a few of the more important substances that have been employed. These are: tar, in the form of oil, ointment, and alcoholic and alkaline tarry lotions; carbolic acid, sulphur, Vlemingkx's solution of sulphurated lime, thymol, ichthyol, hydronaphthol, resorcin, and fluid extract of grindelia robusta. On account of the peculiarity of the eruption, including its multiformity, mixed acute, subacute, and chronic stages, and distressing subjective symptoms, it is difficult both for the patient and physician to estimate the value of any remedy. Such sufferers, moreover, are seldom content to remain long under the care of any one physician, hoping continually to derive benefit from frequent change of treatment. Of the remedies just referred to, the most valuable

is sulphur, and in the form of ointment, about two drachms to the ounce. I was first led to employ it through the statement of a patient many years ago, who had derived more benefit from it than from any other substance. He had suffered long with the vesicular variety, and had sought the advice of many physicians without obtaining even temporary relief. On one occasion, in desperation, he rubbed himself vigorously with a strong sulphur ointment, made soft by the addition of walnut oil. This afforded immediate and gratifying relief, such as no other application had ever given, and, moreover, soon caused the eruption to disappear. On subsequent occasions he had again employed it, and he regarded it as the most valued remedy known to him. The remedy and mode of application seemed to me harsh and unlikely to succeed, but a trial proved satisfactory and bore out the statement made. My experience with it leads me to regard it as especially useful in the vesicular and pustular varieties, and also in the bullous, but that in the erythematous variety it usually proves irritating. Let me here say, however, that in some cases it has failed to act favorably, and I by no means wish to lay too much stress on its value, nor to put it forth as a specific. I merely desire to state that in the vesicular variety it is the best remedy that we are acquainted with. It should be applied with friction and with sufficient force to break down the vesicles, pustules, and blebs as speedily as possible. As already intimated, the ointment should be strong, about two drachms to the ounce, and should be used in the manner indicated, with the view of making a positive impression on the skin, by causing, as it were, local shock to the nerve-endings. The rubbing should be long continued and thorough. It is useless merely to smear it on, as the object by this means is not accomplished. In suitable cases acceptable relief to the itching and burning is usually obtained after one or two applications. Remedies of this class, I believe, are the kind from which most benefit is to be looked for. They should not be too harsh nor too stimulating in their action. The strength and the amount of friction must be regulated by the effect. They should be applied as early in the attack as possible, as soon as the lesions begin to form.

In some cases tar, especially in the form of the alkaline solution known as liquor picis alkalinis, is useful, especially in allaying the itching. It is, of course, to be diluted, one drachm to about eight ounces of water, according to the caustic effect produced. Another equally valuable tarry solution, and one that is safer to use, is that known as liquor carbonis detergens, an alcoholic solution of coal-tar. This also is to be similiarly diluted, though sometimes it may be advantageously used strong, one drachm to from one to four ounces of water. Both of these preparations are useful in relieving itching, but I do not think that they exert much influence in arresting or modifying the progress of the eruption, and hence they can hardly be looked upon as curative. In the erythematous variety they prove of most value, because here the friction ointments are usually not tolerated. Ichthyol I have used in varied strength in the form of ointments and lotions, and, as in the case of tar, the latter have proved more serviceable, but the remedy is not so efficient as tar. Nor can I speak favorably of resorcin, thymol, and carbolic acid. The last-named remedy, especially, has proved less useful than one would expect, considering its well-known powers in other allied inflammatory states of the skin. Of the various remedies and combinations which have been employed on various occasions none can be specially recommended, and hence they need not be enumerated. Baths, for the most part simple and hot, have been used with some benefit in relieving the burning and itching. A patient exhibiting the erythemato-vesicular variety, recently under my care, regarded a hot bath of an hour's duration at night as grateful, but he did not seem to sleep better than when it was omitted. The same patient had, during a previous severe attack, endured a fortnight's experience with the continuous bath, which had afforded a certain amount of ease and comfort, but had not proved in any degree curative.

Concerning the internal treatment not much that is favorable can at present be said. With a disease tending to pursue an emphatically chronic course, speedy cure is hardly to be expected. This observation is borne out by experience. Several cases under my notice some years ago

recovered in a short time under, for the most part, internal treatment, but I am not prepared to state that the cure was due to the remedies used. In the relapsing and obstinate form relief is to be obtained, I believe, only from such remedies as favourably impress the nervous system. The cutaneous symptoms are such as point distinctly to the neurotic nature of the disease. The eruption, as a whole, possesses features in common with the well-known and established neurotic inflammatory diseases, such as herpes simplex, herpes zoster, herpes iris, and pemphigus. The nervous system, it may be centrally or peripherally, is undoubtedly in some manner and in a variable degree deranged, and it is to aid this important function that we must look in the choice of remedies. Among such drugs I would first speak of arsenic, which in suitable cases offers, I believe, more hope of benefit than any other remedy. By suitable cases I mean more particularly the simple, uncomplicated chronic cases, whose history and cause are obscure, and not those manifestly due to a deranged uterus and the like. At the same time, from my experience and from that of some other practitioners with whom I have been in communication on the subject, it must, on the whole, be regarded as disappointing. No reliance can be placed upon it, and sometimes it seems rather to aggravate the disease. Upon inquiry I have found that most of the patients who have been under my observation had at one time or another previously taken a course of arsenic, and without experiencing much, if any, benefit therefrom. I may add that it has often been a matter of surprise to me how little influence for good or for bad it possessed over the disease. While, therefore, some cases seem to have been benefited, the majority have not been so, possibly, in some instances, because the drug had not been administered in sufficiently large doses. In one case, however, very large doses of Fowler's solution (as much as forty or fifty minims a day) were tolerated, and seemed for the time being partially to control the bleb-formation, but the results, upon the whole, were not beneficial. I believe it to be well worth a trial in the vesicular and bullous varieties, and the dose should be gradually increased. From the well-known power of arsenic

to relieve and to cure some cases of true pemphigus, one would naturally look for good results in suitable cases of the disease under consideration, which is, without doubt, allied to the pemphigus process. As far as our knowledge of the treatment of dermatitis herpetiformis extends to-day, no other remedy offers so much hope of benefit in suitable cases, and the results, whether beneficial or harmful, should be duly chronicled with the reports of future cases. Of the value of quinine and strychnine, there is not much to be said beyond that they do not appear to possess any special power over the disease. The same remark may be made concerning certain other general remedies that have been employed —as, for example, iron, cod-liver oil, and ergot. In several cases that are called to mind, it was thought that the hygienic influences of change of air and scene might prove beneficial by giving tone to the nervous system, but in this the results were not commensurate with the trouble incurred. But I would by no means undervalue both moral and hygienic treatment, both of which should receive full consideration; for experience with this disease shows that in most cases general physical and mental depression are conspicuous features.

# THE SENSATION OF ITCHING.[1]

By EDWARD BENNET BRONSON, M.D.,
PROFESSOR OF DERMATOLOGY IN THE NEW YORK POLYCLINIC.

It is a somewhat remarkable fact that a manifestation of cutaneous irritability so common as itching, and one with which as a symptom we are so familiar, has been almost entirely neglected as an independent subject of study. Of other anomalies of sensation, such as hyperæsthesia, anæsthesia, and pain, we have tolerably clear and definite notions. But who has explained for us the cause and nature of pruritus? What is this disturbance of sensation? To say that it is a form of cutaneous irritation that produces an inclination to scratch (for such is the usual definition), is as much as to tell us that itching is the desire to scratch. We itch to scratch, and scratch because we itch. It is clearly a nervous disturbance of some sort; but what produces it, and why scratching relieves it, are questions which, so far as I know, have never been satisfactorily answered.

Itching, or something closely akin to it, is in all probability common to most if not all animals, though most marked in those that are hairy or feathered. Though often provoked

[1] Read before the American Dermatological Association, September 2nd, 1890. Reprinted from the 'Medical Record,' October 18th, 1890.

by irritants extraneous to the body, it also is very frequently spontaneous, occurring under apparently healthy conditions, as well as in disease. When in repose an animal will often by various actions or movements, that answer more or less to the act of scratching, betray the fact that it itches, even when the skin is neither diseased nor molested by insects. And in the human subject spontaneous itching is common enough, and it is often only the sense of propriety that represses the inclination to the desired gratification. The child stripped for bed and begging to have his back scratched is more in the state of nature. Let anyone sit quietly for a moment, fixing attention upon the skin, and the chances are that sooner or later he will become conscious of a slight intrusive irritation at some point, a prickling or picking sensation, and the longer it lasts the more it demands attention. You pass the finger or nail over the irritated point and it is gone. What was it? Was it pain? If all uneasiness is pain, yes. If desire is pain, yes. If the inclination to stretch the limbs, to wink the eyes, to eat is pain, so is this trifling disturbance of sensation, this desire to scratch.

In severe itching, and especially in disease, the feeling becomes more complex. This is evident from the multiplicity of expressions used to describe it—such as "tickling," "prickling," "picking," "creeping," "crawling." But always there goes with it the impression of intrusive contact, together with the longing to scratch. Closely connected with it are other sensations that are secondary and probably entirely independent of the feeling of itching. Such are the smarting, burning, or stinging sensations which only accidentally are coincident with this feeling, and are clearly painful sensations. They are not only independent of the pruritus, but are distinctly antipathic to it. As soon as the scratching becomes violent enough to produce a painful sensation the itching is, temporarily at least, extinguished. Furthermore, any painful sensation of the skin would most likely be aggravated by scratching. Though pruritus has sometimes been described as a variety or phase of pain their characters are totally dissimilar. The feeling of pruritus always carries with it the suggestion of something extra-

neous to the body. There is in the sensation an element of objectivity, while in a painful sensation the feeling is purely subjective. In the one there is the consciousness, whether deceived or not, of something outside of self. In the other, one is only conscious of the suffering. One is resentment, with the instinct to repel an attack, an intrusion; the other is a suffering self-consciousness without cognizance of the producing agent. One is a longing desire to resist; the other the passive endurance of penalty.

Though a certain consciousness of the agent may accompany pain, it is very different from that in pruritus. One resents a stinging blow, as the lash of a whip. The soldier struck by a spent ball curses the enemy. But there is no consciousness of the presence of a whip in the smarting flesh, nor of an enemy in the aching limb. Cause and effect may be a mile apart; it is only the effect that remains, and of that only is the subject directly conscious. At the first instant of injury, the organ of touch is sufficiently involved to give intimation of the locality injured, and perhaps something of the quality of the injurious agent, but the sensation of pain *per se* gives no such intimation. It is simply a passive condition. In pruritus, on the other hand, cause and effect are presented to consciousness as one. The consciousness of the object, the irritant, is not an instantaneous intimation, but persists while the itching lasts.

But if pruritus is not pain in the ordinary acceptation of the word, is it any more nearly related to the special sense of touch? What are its relations to the so-called special senses on the one hand, and to common sensation on the other?

The distinction recognised between common and special sensation is that, while the former communicates only impressions of subjective states of the body, the latter imparts knowledge of external things. Through the former we are made aware only of somatic conditions, changes or phenomena that transpire in the *ego;* while through the latter we take cognisance of changes or phenomena in the outside world, the *non ego*. By means of the special senses the presentations to consciousness are such that we are enabled to appreciate the qualities of external objects, and through a

series of such presentations to know, to perceive, what the thing producing the sensations is. Such definite and competent sensations, perceptive sensations, exist only in connection with the senses of seeing, hearing, smelling, tasting, and touching. All other sensations, though widely diverse in character among themselves, are little more than varying phases of ease and discomfort, of well-being and ill-being, of desire and gratification. Except through association of ideas, through imagination, they have no connection in consciousness with the outside world.

But notwithstanding the fact that the special senses in their present state are so far removed, in respect to the knowledge they yield to consciousness, from common sensation, there doubtless was a period when the distinction did not exist. Their differentiation has been the result of gradual and long-continued processes of evolution. There can be little question that the sensory organs, to which the several senses owe their special attributes, have all originally developed from simple nerve-endings that could give but the vaguest intimations of external objects. At the very beginning there was simply a common sensitive exterior that reacted to the various irritations it encountered in general, and more or less indefinite movements of the protoplasmic mass. Beginning with the protozoa, the protrusion of pseudopodia, as in the rhizopoda, was among the first simple attempts at adaptation. In further progress, and by a similar process, tentacles and sensitive hairs appeared. Nerve-terminals, at first homogeneous, gradually resolved themselves for division of labour in special organs. From the common sensitive exterior there were separated in the course of time the optic and auditory vesicles, with nerve-filaments distributed over their interiors. Over little clefts or depressions in the integument other nerve-filaments became differentiated, as the organs of smell and taste ; while the common integument, retaining its primitive common sensations, evolved a special sense of touch. The facts of evolution are exactly reflected in the parallel development of the embryo. Out of the ectoderm or outermost germ-layer the organs of special sense are gradually developed, and traverse the same general phases of progress, as may be traced in the

evolution of the higher creations of the animal kingdom. Both ontogenetically and phylogenetically the simple origin of the organs of sense appears too obvious for dispute. Diverse in their individual characters, as well as in their divergent routes of descent, as these organs are, they all converge toward a common source in a general sensitive exterior composed of homogeneous nerves.

The earliest attempts at specialisation in this common sensitive exterior could have effected little more than certain modifications of common sensation. To fix the exact period when these primitive modifications began to develop into the special senses, through which the animal is placed in intelligent communication with its environment, is needless, if it were possible. It must in general correspond to that period when the animal's movements first showed indications of purpose. When the amœba comes in contact with a foreign substance the reflex movements that are excited are vague, haphazard, and apparently purposeless. According as the contact occurs, or as the object is presented to it, the animal shrinks away from it, or contracting about it envelops it in its interior, where, should the substance happen to be nutritious, it may be absorbed. The first beginnings of adaptation would naturally be associated with the simple consciousness of contact, a sort of primitive sense of touch. With the first intimation to the animal of a difference between one kind of contact and another, we reach the threshold of an objective consciousness and the commencement of perspective sensation. Partly empirically and partly through natural selection the differentiation of sensation gradually proceeds. The animal now directs its movements with intelligence and purpose. It acquires the ability not only to feel but to perceive. It can select and seek its food, evade or attack its foes, and so gradually is equipped for the struggle for life. Thus, as all the sensory organs can be traced to one elementary and homogeneous organ, so all sensations, whether common, special, or perceptive, may be traced to one undifferentiated and elementary sensation, which is common sensation.

In this evolution the impelling force, the directing impulse, has been derived from the two grand principles of

life known as the instinct of self-preservation and the instinct of reproduction. To one or the other of these instincts every sensation that arises in the body must be directly or indirectly referred. All sensations, as we have seen, were originally tegumentary. To the common integument must be ascribed the source and potentiality of all sensations. As the result of specialisation, most of these sensations have been withdrawn from the exterior. What traces of the special senses thus abstracted still persist in the skin may be infinitesimal. That such traces do exist there can be little doubt. At least, that the skin is sensible to waves of light, has been demontrated by curious experiments. There still remains to the skin and adjacent mucous orifices a variety of sensations, some of them undifferentiated from the elementary common sensation, others more specialised, including a special sense with perceptive faculties, and, finally, the most important representative of the reproductive instinct, the aphrodisiac sense.

The objective or perceptive sensations of the skin constitute what is known as the sense of touch or tactile sense. It is the sense by which we apprehend the form, size, location, temperature, and various other qualities of external objects, such as softness, hardness, smoothness, roughness, and the like. Many of its attributes it owes to the so-called muscular sense, which in many tactile operations cannot be disassociated from the sense, of touch. Moreover, the sense of temperature is really an independent sense, depending actually upon nerve-terminations, especially adapted to this purpose. This independence has long been recognised in certain pathological conditions, where one sense has been annulled irrespective of the other, while the recent experiments of Goldscheider have established the fact still more positively. Goldscheider, having first established experimentally that there were certain areas of the skin sensitive to touch and others to temperature, on excising these areas found microscopically that the innervation was also distinct.

Of the existence of a specialised sense of touch there is no question, nor that it is limited to the skin and adjacent mucous orifices. It is not wholly expressed by pressure

nse, for it is incomplete without the accessory muscular nd temperature senses. Again, there is a sense of contact, he sense of being touched without perceptible pressure, which has come down from the earliest periods of animal development, and which, originally at least, must have been unassociated with tactile sense as we now understand it. Before any consciousness of pressure exists we are sensible of contact. But something more than this is necessary before there can be anything like sense of form or quality. It is this sense of contact, doubtless, that is the beginning —the threshold of pressure sense.

What is meant, then, by the phrase "sense of touch"? As we have seen, it has a composite character, but, though made up of heterogeneous elements, the perceptions that flow from it are as definite and as distinctly individualised as those afforded by its sister senses. Nevertheless, the term is a vague one, and inadequately expresses the sense implied. As we have seen, simply touching an object, simple contact, evokes a sensation or sensations that are only preliminary to the specialised sense. We become conscious of local contact before any quality of the object touched can be distinguished. It is only when the feeling of resistance begins and we are aware of pressure that there can be any appreciation of quality. It may be said that such appreciation is purely an intellectual act; but as the brain would be incapable of appreciating the different tones in sound except for the organ of Corti, or the different colours of the spectrum except for the intervention of the retina, so is it probable that the tactile perceptions would not exist but for the presence of special sense organs in the skin. Such organs have been aptly termed "organs of reinforcement."

The expression, therefore, for the special perceptive sense that belongs to the skin should imply more than mere touch. It is not simply sense of contact, it is not simply feeling, but it is contact *plus* something else; it is feeling *of* the object as well as simple feeling it. The word palpation better expresses the act whereby the sense is evoked, but etymologically that term would be too restricted. Palpation (from *palpus*, the palm) relates more particularly to manipulation; it is feeling with the hand only. A still

better term would be pselaphesia. The Greek ψηλάφησις conveys the idea of feeling for or of a thing, or groping as a blind man or as one in the dark. The Latin *tactus* (from *tango*), on the other hand, signifies only the act of touching, as expressed in the words tangent and contact. The only sense with which the skin is endowed that can properly be called perceptive, and that is worthy of comparison with seeing, hearing, smelling, and tasting, is the sense of pselaphesia. It includes the sense of contact, which, as we have seen, is its most primitive form; its more important element is pressure sense, while the temperature and muscular senses are more or less essential auxiliaries. Common sensation is represented in the integument in its highest positive aspect by the voluptuous sensations; in its lowest negative aspect by pain.

From analogy with its sister senses, the sense of pselaphesia should depend upon a special arrangement and adaptation of the nerve-endings. There should be an organ or "organs of reinforcement." It is scarcely probable that in the skin there is any such highly specialised arrangement as in the eye and ear, and yet we find nervous structures in the skin whose distribution and peculiar development mark them as organs of special importance to cutaneous sensation. What the exact functions of these different structures are is yet uncertain. It is little more than conjecture what special parts are played by the corpuscles of Meissner or those of Pacini, by the terminal bulbs of Krause, the nerve plexuses beneath the epidermis and about the hair-follicles, the tactile cells of Merkel, the free nerve-endings, and, finally, the nerve-distributions to the epidermis, including the remarkable intracellular nerves described by Pfitzner and Unna. Suffice it for the present to say, that from analogy we should expect the most highly developed of these to correspond to the most highly developed sense, to pselaphesia.

To turn from this long, though not purposeless digression, what relation to all these sensory organs of the skin and to their various sensations does the sensation of itching bear?

First of all, the sensations of pruritus must have to do with nerves that are very superficial. There is no reason to

believe that of pressure sense, properly so called, there is the slightest intimation. If, with the end of my pencil, I gently approach a sensitive surface, such, for example, as the cheek or one of the alæ nasi, I become aware of a sense of contact the instant the surface is touched. A little pressure and I receive the impression of a smooth, rounded body, and a moment later a slight sensation of coolness. I have a perceptive sensation. If, instead of making any pressure, the pencil be retained just at the point of contact, presently a feeling of annoying irritation is excited. Still more marked is this irritation if, instead of using the pencil, the part be lightly touched with a pointed wisp of soft paper or feather. There is elicited directly the sensation of a minute local shock, associated with an instinctive desire to escape from the irritating cause. If the same be repeated the excitement of the part becomes so great that the desire to rub or scratch it becomes almost irresistible. This sensation is pruritus, and it is evidently a nervous disturbance provoked by touching the sensitive surface. What and where is this disturbance, and why should it be apparently so much greater than would be produced by a much more forcible contact?

First, how is it related to pselaphesia? The certain amount of pressure necessary to evoke this special sense implies that the organs on which it depends lie deep in the skin, and are doubtless those highly developed nerve-structures that are situated below the epidermis. It is evident that whatever connection the mere sense of contact may have with these organs it does not bring them actively into play. It is a well-known fact that in certain pathological states apselaphesia may coexist with hyperæsthesia of the surface, *i. e.* an exaggerated sensitiveness to impressions of contact. Moreover, those areas of the body most highly endowed with special tactile sense, with the sense of pselaphesia, are by no means necessarily the ones most sensitive to contact; nor are they to pruritus. While itching has no apparent connection with the sense of pselaphesia, it cannot be dissociated from the primary sense of touch, the sense of contact. Now, obviously, this sense of contact should pertain to those nerve-endings but slightly differentiated and those

most superficial. Such nerves exist in abundance in the epidermis.

While I can present no absolute proof of the proposition, I believe there is sufficient evidence to locate the essential seat of pruritus in the epidermis. Itching is evoked by such irritants as act upon this tissue much more uniformly than by those that act on the derma. We have seen how it may be excited by external irritants that barely touch the surface without the least intimation of a pressure sense. The itching that is commonly observed in connection with the healing of superficial wounds is not attributable to the granulating process. There is no itching in the granulations of an ulcer. It is only when the part begins to heal and to "skin over" that the itching begins. It is a symptom of keratoplasia, not of dermatoplasia. In those cutaneous diseases also that more especially affect the derma, itching is present only exceptionally. In the erythematous, erysipelatous, and phlegmonous inflammations the sensations are of a smarting, burning, or aching character, *i. e.* painful sensation, and if ever pruritus it is because of secondary implication of the epidermis. Likewise, of papular affections, as, for example, in syphilodermata, that are characterised by infiltrations confined to the corium or papillary body. If itching occur it is due to a similar and accidental implication. On the other hand, the essentially pruriginous affections, such as eczema, pemphigus, scabies, or lichen planus, are those invariably associated with decided trophic changes in the epidermis. In urticaria the implication of the epidermis is not so obvious, but, as shown by Unna, urticaria is not primarily or essentially an inflammatory disease. It is often a neurosis, and the itching is the primary factor, an irritation reflected to the terminal nerves from the nervous centres. The œdematous effusion that accompanies it, together with the local ischæmia, is doubtless the direct effect of muscular spasm.

However provoked, the sensation of itching is always associated with a presentiment to consciousness, as though a foreign body were in contact with the surface. It is that sensation that experience through many stages of animal life has taught is often followed by a prick or a sting, and the

inclination to escape the threatened hurt has grown into an animal instinct. The sense of contact at a minute portion of the sensitive surface is immediately interpreted to mean a miniature attack that must be repelled. If no attack has really been made, but only the threat, the intimation, then the excitement should disappear without returning the moment the cause producing the sense of contact is withdrawn. But it is the peculiarity of itching that it persists in spite of such withdrawal, and is only relieved by the act of scratching. It seems as though the contact, or whatever the change may be that gives rise to the irritation, produces a molecular commotion in the nerves that goes on like the jangling of an electric bell, with a continuance of the sensation until such time as the surcharge of nervous energy is released. In pselaphesia the nerve-force, or the molecular vibrations excited by the impact, is directly transmuted into some intelligent form of activity, and the accumulation of nerve excitation—the nervous engorgement—does not occur. The circuit is complete, with no point of resistance intervening to create obstruction, and so commotion.

With regard to the sensations of pain, the view was maintained by Funke[1] that they passed into the gray tracts of the spinal cord, where their further progress was arrested; while tactile sensations (the sensations of pselaphesia) traverse the less resisting white tracts, and thence passed directly to the brain. Whether this explanation would apply also to the sensation of itching, whether the obstruction that produces it is the same as for painful sensations, is a question that can neither be affirmed nor denied. It may be that the same process which produces what is called pain, when proceeding from nerves deeply seated, becomes itching if it starts from the nerves of the epidermis. Or, on the other hand, it might be alleged that the only difference lies in the amount or severity of the irritation, the nerves involved being the same. There are reasons, however, for believing that the epidermic nerves are not susceptible to pain. If with a knife we gradually pare away the epidermis, or if we thrust a fine needle through it, no pain is pro-

[1] See in 'Hermann's Physiology' (1879, iii, 2), "Physiologie der Hautempfindungen und der Gemeingefühle."

duced until it reaches the papillary body—until it "goes to the quick," as the common phrase is. But it may be objected that neither does this cause itching. The explanation is easy: An essential condition to the production of pruritus is the uncertainty, the vague and indefinite character of the sensation. The impression that the knife or needle produces as it forces its way through or between the cells of the epidermis is one which offers a clear and interpretable presentment to the sensorium; the sensation undergoes immediate transmutation into other forms of nerve-activity, thus obviating the accumulation or stasis of nerve-force. It is a definite and perceptive sensation, which doubtless calls into play the special organs of pselaphesis that may serve to turn the course of the molecular vibration into the direct channels of the spinal cord. *A priori* reasons for differentiating pain from pruritus have been given already. We have seen that they are not only inconsistent with, but antipathic to each other. The means to which the animal instinctively resorts for their relief are distinctly opposed to each other. While pain demands rest, pruritus incites to action. It is also probable that they engage distinct elements of the nervous system.

The reflex muscular movements excited by itching doubtless had for their object originally the expulsion of a foreign body, often an insect. Such movements are frequently spontaneous and more or less unconscious. Analogous responsive muscular movements are seen in sternutation and the act of coughing. The tickling sensations of the nasal or laryngeal mucous membranes which are their provocation correspond very closely to cutaneous itching. But the relief afforded by sneezing is not wholly explained by the expulsion of the irritating substance, but, partly, by the fact that the effort affords an avenue of escape for the retained nerve-force, a means for the transmutation of this force into muscular energy. In those animals in which the platysma myoides is more highly developed than in man, as in the horse and bovine genera, a certain relief may be afforded to pruritic sensation through its energetic contractions, which is not wholly due to expulsion of the insect or whatever else may have caused the sensation. The same ten-

dency to dissipate pruritic irritation through liberation of muscular force is evinced in the cutis anserina as well as in the hypertrophy of the arrectores pili muscles observed in many pruriginious diseases. May it not be that the changes in urticaria are the consequence of misdirected and ineffectual efforts of the cutaneous muscles to expel an irritant that produces on the sensorium the counterfeit presentment of some tangible body, as it were an offensive insect?

With regard to the effect of scratching in relieving itching, it is analogous to that produced by muscular exertion. Both cause a deflection of the pruritic irritation into other and freer channels. In the action of scratching there is substituted a decided and definite sensation for one that is simply vague and incomplete. It is the substitution of an effective energy for an ineffectual vexation.

Thus we arrive at something like a rational explanation of what itching is, why the sensation is attended with greater perturbation than are sensations produced by more tangible and appreciable contacts, and, finally, why it is relieved by scratching. Inasmuch as the presentations it yields to consciousness are vague and indefinite, it is closely related to common sensation; but inasmuch as it contains the glimmerings of an objective sense, it is just one stage removed from it. It concerns those primitive nerves of contact out of which originally were developed the organs of special sense. It disturbs sensibility that was the precursor of, and doubtless is preliminary to, the sense of pselaphesia. Inasmuch as it concerns a sense of touch, it might be characterised as a paræsthesia of tactile sense; but regarding it more particularly as a disturbance due to interference with, to obstruction of, sensation, a condition in which there is vexation and annoyance of consciousness through the very indefiniteness and uncertainty of the sensations, the word paræsthesia does not express enough. Unfortunately, a term that most fitly expresses this condition has been already appropriated. Charcot has given the name "dysæsthesia" to a form of hyperæsthesia or paræsthesia occurring in myelitis, in which slight irritations of the surface, such as pinching, or the application of cold, are directly followed by painful vibratory sensations coursing up and

down the region irritated, and often appearing symmetrically on the other side of the body, and that continue for a considerable time after the irritant has been withdrawn. In some respects the dysæsthesia of Charcot corresponds to the phenomena of itching. At all events, the term employed is, etymologically at least, as appropriate to pruritus as to the painful sensations just described.

To explain in detail, or even enumerate all the different phases of itching would be impossible. While some of them are associated with pathological changes in the epidermis incident to certain cutaneous inflammations, others have their source more deeply situated and are referable to the nerve-centres. To the latter belong the form of neurosis, of which pruritus is at the same time the symptom and sole appellation. Still, other sources are doubtless to be found associated with apparently normal physiological conditions. It would seem as if a certain amount of scratching were, under some circumstances, salutary and requisite for an animal's integument, and that the sensation of itching were the necessary incitement. It would facilitate the fall of deciduous hairs, it would promote the normal exfoliation of the cuticle, which, under certain conditions, may not separate rapidly enough to permit the upward growth and expansion of the prickle-cells of the rete. It would tend to dislodge accumulations in the crypts of the skin, the sweat, and sebaceous follicles. While these represent the most obvious sources of itching, or provocations for scratching, there is another factor of which hitherto but little account has been taken.

Both the English words itch and itching and the Latin prurio and pruritus, in their secondary significations, convey the idea of a longing, teasing desire. It is apparent in such expressions as "the itch for gain," "the itch for praise," "the itch for scribbling;" while pruritus was commonly used by the Latins as a synonym for lasciviousness. There is an element of desire in the sensations of itching, and it is not improbable that the common, more or less definite recognition of this element is accountable for the derived or secondary meanings just alluded to. By desire in this connection, something more is meant than merely the inclination to brush or scratch away a foreign body, of which the

sensation is apparently an intimation. It is, rather, a kind of desire closely akin to a lustful feeling, and one that sometimes makes scratching veritably a sensual indulgence. When pruritus reaches a certain degree of intensity, the subject is not content with that moderate amount of scratching that would ordinarily create a sufficient diversion to give relief, but there is a disposition to attack the itching surface with a vehemence that amounts to passion. Observe the motions of a dog when scratching. Sometimes its violent movements and muscular exertions betray an agitation that is not unlike the excitement of the sexual orgasm. The very act of scratching appears to evoke a condition of erethism and excitement that is far in excess of the mere pruritic irritation. And in the human subject voluptuous feelings are not infrequently accessories to the sensation of itching. The delight of having one's back scratched is doubtless chiefly due to a longing for a voluptuous gratification that would not exist but for the pruritic titillation. When the scabious Scotchman at the "scratching-post" fervently ejaculutes his "God bless the Duke of Argyle!" it is not only the negative satisfaction of relief that he feels, nor that combined with clannish loyalty, but his sensations include an element of positive enjoyment, he is having the pleasures of a gratified sense.

Recognising this peculiar element of desire in pruritus, the sexual excitement and depraving tendencies that are so commonly associated with pruritus genitalium are most easily explained. But it is not so surprising that voluptuous sensations should attend itching here where they have their natural seat. Such sensations, however, are not confined to the genitals. They also affect the anus, where, more especially under certain conditions of moral perversion, as well as in association with pruritus ani, the erectile tissue in this situation may become the seat of erethism, and in a measure there is excited an aphrodisiac sense. The female nipple also is susceptible to voluptuous sensations. These facts are well known, but the more general distribution of such sensations has received little consideration. They may be concomitants of itching in almost any situation. Persons subject to pruritus of the external auditory meatus are often in

the habit of introducing the tip of the finger into the ear and making rapid vibratory movements that do not merely quell the itching, but produce sensations that are distinctly voluptuous. The same is true, if in a less degree, of excessive rubbing or scratching of any surface that itches. There must be, however, the provocation of the pruritic irritation. By means of a violent excitation, superinduced by severe scratching, a liberation or discharge of nervous energy takes place, accompanied by pleasurable sensations, together with the relief of the pruritic irritation. A temporary inertia and rest follows and continues till a renewal of the pruritus provokes another resort to the same method of relief. How is this voluptuous feeling explained ?

We have already seen that the only special senses that remained to the common integument after the differentiation of the special senses had taken place were the tactile senses, including the senses of contact, of pressure, and of temperature and the aphrodisiac sense. We saw also that the special sense of pselaphesia, while most highly developed in certain parts, existed to a greater or less degree over the whole surface. The same thing would seem to be true in a measure of aphrodisiac sense. Like the former, the latter is but a higher development of the primitive sense of contact. It has a special organ or instrument—the penis in the male, the clitoris in the female—much as pselaphesia has as its especial organ or instrument the hand; moreover, like the latter sense, though perhaps in a less degree, it is distributed over the entire cutaneous surface. Now, sexual excitement has for its incentive the desire to gratify a special appetite, the agent or vehicle of which exists in the cutaneous nerves of contact. A plethora of nervous irritation is generated in the communicating nerve-centres, which can only be released by a violent general agitation, an explosion, as it were, of nerve force, which is followed by equilibrium or by a minus state of depression. This is the sexual orgasm. The whole process is in close analogy with what we observe in connection with the relief of the intenser forms of itching by violent scratching. In each case the stored up energy has to do with the nerves of contact or the centres with which they directly communicate. These are the non-con-

ductors that accumulate and retain the charge; the motory apparatus furnishes the channels through which the charge is conducted away in muscular energy.

As to why this process is attended with pleasurable sensations, it suffices to say it satisfies a law of being. Gratification of appetite is a condition of life, either of the preservation of life or of the reproduction of life. The sexual, the aphrodisiac appetite can only be secondary to the instinct and appetites of self-preservation. It is the outcome of superabundant vitality. With the surplusage there is engendered the instinct, the impulse to increase, to give life, to make more life. The acme of this impulse is passion. When the increments of vital energy reach high-water mark there is tumultuous overflow, as in the syphon of an invisible spring.

It is not only in the aphrodisiac sense that this impulse is displayed. It actuates many of the highest intellectual and emotional faculties of man. Through it the mind conceives and reproduces; the purest sentiments of love are its offspring. In the control of all the forces, both of the body and of the mind, the reproductive instinct shares with the instinct of self-preservation, the one being the opposite and the complement of the other, as in the conduct of life the spirit of altruism is the opposite and complement of the spirit of egoism. The one prompts to give more than it gets; the other to get more than it gives. The one dissipates energy; the other conserves force. One or the other of these two great instincts provides the mainspring of every human action and is the source of every animal appetite. Their combined product is life. Aphrodisiac sense, the lustful sense of contact, is but a phase, a single factor in the great domain of the instinct of reproduction. The appetite it engenders, the lust of the flesh, at the same time the most ignoble and the most dominating appetite of exuberant animal life, is but a means to the grand end, and when prodigal nature established its chief seat and "sacred" organ, she neglected to withdraw from the outlying regions of the general surface those traces of a congenetic sense that remain in a more or less primitive form, but nevertheless engage corresponding elements of the nervous system.

From the foregoing considerations I believe we are warranted in drawing the following conclusions :

I. That there is a sense of contact independent of the sense of pselaphesia.

II. That this sense of contact is the sense disturbed in pruritus.

III. That it concerns primarily, simple cutaneous nerves or nerve-endings, situated superficially and probably in the epidermis.

IV. That the disturbances in pruritus is of the nature of a dysæsthesia due to accumulated or obstructed nerve excitation with imperfect conduction of the generated force into correlated forms of nervous energy.

V. That scratching relieves itching by directing the excitation into freer channels of sensation, sometimes, especially when severe, substituting for the pruritus either painful or voluptuous sensations.

VI. That the voluptuous sensations that may attend pruritus are a manifestation of a generalised aphrodisiac sense, representing a phase of common sensation that has its source in the sense of contact.

# REPORT OF A CASE

OF THE

# MYCOSIS FONGOÏDE OF ALIBERT.[1]

By HENRY WM. BLANC, M.D.,
DERMATOLOGIST TO THE CHARITY HOSPITAL, NEW ORLEANS.

THE rare affections of the skin first described by Alibert under the name of Mycosis Fongoïde, and of which he gave an illustration in his atlas more than half a century ago,[2] has of late years been described by a number of observers under a variety of titles. Among the Germans we find the name *granuloma fungoides* to prevail; the French prefer to call it *lymphadémé cutanée;* while the Americans recognise this disease as the *inflammatory fungoid neoplasm* of Duhring. But these names are simply tentative, and even the inventors of them confess that all designations will remain imperfect and unsatisfactory until the true nature of the affection is understood.

Independently of the one here reported, it has been my good fortune to have observed two other cases of this disease within the past four years. One of these was in the service of Prof. Geo. H. Fox, at the Skin and Cancer Hospital, New York; and my position there as house physician

[1] Reprinted from the 'Journal of Cutaneous and Genito-Urinary Diseases,' vol. vi, July-August, 1888.

[2] 'Clinique de l'Hôpital Saint-Louis, ou Traité complet des Maladies de la peau,' Paris, 1883.

permitted daily observation for several months, during which time the most careful notes were taken. The other case observed by me was under the care of Prof. Stephen Mackenzie at the London Hospital, in the summer of 1886;[1] and I had the satisfaction of having my opinion as to its nature confirmed later on by a number of prominent specialists.

In the clinics and hospitals on the Continent I saw no examples of this disease; but the exquisite wax models of M. Baretta at the Hôpital Saint-Louis, Paris, were sufficient to convince me that the two cases just referred to, and the one here reported, are very closely related to those figured by the French dermatologists.

The patient whose disease is now to be described, was admitted into my service at the Charity Hospital on August 10th, 1887, with the following history:—White man, æt. 34; native of Germany. Occupation was that of a tailor in New York City previous to 1883. Is of blonde complexion, and was formerly quite fair. While in Mound City, Kansas, in May, 1883, a scaly and itchy eruption, unaccompanied by any discharge, appeared on legs. In about four months this "dry tetter," as he calls it, broke out on the hands also, when rhagades appeared on the palms, and the eruption began to discharge.

It then spread to the breast and arm-pits; the hands in the meantime becoming so much improved that he could work again at his trade. This he continued to do until the spring of 1884, when there appeared on the body a number of "red blotches covered with yellow pimples which contained a little black spot in the centre." He then entered a hospital in Omaha, where he remained about twenty-one months, suffering with a disease which was called "general eczema," and pronounced non-contagious by the physicians. Patient states that while he was in the Omaha Hospital the hair of his scalp, eyebrows, lashes, and beard all fell out, but had begun to return before he left the institution in March, 1886.

The eruption disappeared while he was in this hospital,

[1] Neither of these cases has yet been reported, as far as the author is aware.

but the skin remained red and tender, and continued to itch over its entire surface. Departing for Quincy, Ill., in June, 1886, he was there able to pursue his vocation until the middle of January, 1887. At this time he had a swelling of the feet which resembled frost-bite, and the toes were cut and cauterised by physicians of the place. Remaining under medical care until April 13th, 1887, he then came south by advice, stopping for a short time at Hot Springs, Ark., where he took frequent baths which were always followed by chills.

He then came to New Orleans, and under my observation.

*Condition on admission.*

When admitted to the hospital the patient was very weak, nervous, and emaciated, and was compelled to take to his bed. Two facts about him were particularly noticeable; one was the great number of multiform tumours covering his trunk and extremities, and the other was an extremely disagreeable and pungent odour emanating from his hands and feet.

*Head.*—The skin of the face was slightly thickened, especially about the eyebrows, which were scanty and nibbled off in places as in ringworm of the scalp. The skin was flushed, the nose red, and expression of face nervous and uneasy. Beard straight and growing only from the chin, though, according to his statement, it had been much thicker before he pulled it out when loose from inflammation in the skin. Scalp pale and covered with fine dry scales. The only tumour on head was one the size of a buckshot, just within the meatus of left ear. Tongue and throat normal, but projecting from the hard palate was a purplish tumour the size and shape of a filbert, which had been as large as an English walnut several months before, and seriously interfered with deglutition. On the neck just below chin was one small sessile tumour.

*Trunk.*—The skin of the trunk, considerably pigmented in the abdominal region, was covered indiscriminately with forty distinct tubercles and tumours. While some of these growths were merely hard, purple deposits, slightly raised

above the skin, others formed sessile or pedunculated tumours that could be caught up between the fingers. The average size of these was that of a split cherry.

*Upper extremities.*—The skin of the upper extremities was rough, scaly, and slightly pigmented from the irritation of constant rubbing. On the right arm and forearm were twelve tumours distributed over the surface. The majority were about the size of a pea, and projected prominently above the skin; while two or three, a little larger than the rest, projected from eight to twelve lines above the surface as raw, elongated growths, with narrow pedicles, and which secreted an ichorous fluid. The right hand was much swollen, and covered with red, thick skin. In the palm of this hand were three pedunculated tumours the size of a cherry. The fingers were stiff, and could be moved only with pain and difficulty. They were about three times as large as normal, and covered with a fungous mass of a purplish-blue colour, soft to the feel, and irregular in shape, being larger at the distal extremities. This outgrowth on the fingers was most marked on the terminal phalanges, where it was heavier and more nodular, obliterating the outline of the digits, which could only be recognised as such by the presence of smooth, clubbed nails, that projected through the mass undisturbed by the disease. The general appearance of the left upper extremity was like that of the right, except that the tumours on the arm and forearm were about sixteen in number, the largest being about the size of a filbert. The left hand closely resembled the right in appearance, except that it was less swollen, and had the first phalanges of the third and fourth fingers free from disease.

*Lower extremities.*—The skin of the thighs and legs, particularly the former, was covered with whitish scales and much roughened by rubbing. Innumerable papules, and many prominent tumours the size of a cherry and larger, studded the surface of the thighs and legs. One tumour on the left thigh, just below the trochanter of the femur, greatly resembled a door-knob in size and shape.

The most remarkable appearance presented by the disease was seen upon the feet, from the dorsal and plantar surfaces of which projected fungous masses resembling in-

ternal hæmorrhoids more than anything else, except that they were more of a purple hue. These tumours, when not flattened to the skin by bandages, projected in several instances at least an inch and a half from their attachments, and were very narrow and flat. The toes, though present, could not be distinguished in the mass of fungous growth that projected from the end of the tarsus; though the interlacing nodes could be separated from one another by careful manipulation. The toe nails, unlike those of the fingers, were displaced and deformed, being turned upward towards the dorsal surface of the foot. None of the nails were missing.

The very fœtid odour already referred to was due to a sero-purulent discharge from the hands and feet, particularly the latter; and originated in the thin membrane-like surface of the fungous masses, which constantly poured it forth without well-defined ulceration. On examination the lymphatic glands were found to be notably enlarged, more especially the axillary, epitrochlear, femoral, and inguinal, all of which could be detected with the eye as well as by sense of touch. In addition to these the following could be distinctly felt, and in several cases seen:—the zygomatic, post-cervical, dorsal (just outside of the axillary border of the scapulæ), and the thoracic glands at the lower border of the pectoralis major muscle. Several smooth red patches on the skin were declared by the patient to be the remains of tumours which had just disappeared, similar processes of resolution having frequently occurred in his history since the frost-bite in January, 1887.

Examination of the internal organs disclosed no special form of disease, and the spleen could not be felt beneath the abdominal walls. The patient was in a very nervous condition, jumping if any of the tumours were touched, and complained of intense itching, particularly at night, in consequence of which he kept up a continual rubbing of the skin at all times. The appetite was poor and bowels moderately regular. Urine examined chemically and microscopically, and nothing abnormal found. Specific gravity 1010.

Such was the case as it first came under my observation. Recognising in it a rare disease, and believing it to be

similar to the two cases already referred to, I determined to administer iron and arsenic with the idea of increasing the blood-cells and improving the nutrition of the skin. Being about to leave the city on a six weeks' vacation, I ordered the following mixture, to be continued, if practicable, until my return :

℞ Ferri et Quiniæ Citrat., ʒij ; Liq. Potass. Arsenit., ʒj ; Syr. Aurant. Cort., ℥j ; aquæ, q. s. ad ℥ij. Dose a dessert-spoonful three times a day after meals. This was administered in my absence, and no other directions given, except for a powder of ten grains of hydronaphthol with half an ounce of bismuth to be applied to the discharging surfaces on feet and hands. This powder did good service, and greatly diminished the fœtid odour.

During my absence small specimens were cut from the tumour of the foot and sent to the pathologist, Dr. Schmidt, with the request that they be examined for the bacillus lepræ. The report showed, as might have been anticipated, that not only were there no bacilli, but that the neoplasm did not in the least resemble deposits of leprosy. On my return frequent notes were made of the case, and I shall endeavour to give those that best show the progress of the disease.

*Clinical History.*

November 15th.—Patient has been taking arsenic and iron for three months, and shows decided improvement in skin lesions. The tumour in mouth has diminished to the size of a pea, that on thigh is now the size of a hazel-nut, and several small ones on the arms and legs have disappeared altogether, leaving no cicatrices, and very slight pigmentation. Hands are less swollen, and have lost their raw appearance ; feet discharge less, and are not as tender. Ordered ichthyol (sulpho-ichthyolate of ammonium) and vaseline, equal parts, to be applied constantly to fingers and hands.

25th.—Thickening of fingers has notably diminished under use of ichthyol. On removing a tumour for microscopical examination great nervousness was produced, fol-

lowed by a chill and slight elevation of temperature, after which patient perspired freely. These nervous chills have occurred several times of late, particularly after a handling of the tumours or stripping of the patient for examination. The temperature seldom rises higher than 100° during what he calls his "fever attacks," though he perspires profusely after them, the face remaining redder for two or three days at a time. Says he has sensations similar to these, but milder, after the feet are dressed in the evening. The fever is easily controlled by cinchonida. Intense itching is a constant symptom.

December 12th.—Had one of his nervous attacks, followed by sweating and great prostration, after being removed to another part of the hospital to be photographed. Hands are looking well, but feet have been painful of late. Substitute the following for the hydronaphthol mixture on feet: Iodoform, Bismuth. Subnitrat., āā ʒj. M.

January 16th.—Tumours on the trunk have decreased to ten in number; and those on extremities had ceased to grow until two weeks ago, when diarrhœa set in, and arsenic mixture was temporarily stopped in favour of opium and bismuth internally. Several tumours have rapidly increased in size and taken on a fungoid appearance since discontinuance of the arsenic. But bowels have improved, and arsenic is now resumed with twenty grains of subnitrate of bismuth at a dose. As the feet are better, it is determined to try the effects of ichthyol in place of the powder of December 12, though this has given great relief: Ichthyol, ʒss; Iodoform., ʒiss; Vaselin., q. s. ad ʒij. M.

27th.—Feet are swollen, and ichthyol discontinued in favour of hydronaphthol powder, which has been most successful in drying and deodorising the surfaces. Face remains flushed now, but tip of nose is less red. Tumour in mouth has entirely disappeared, and nothing remains but a dark spot the size of a pea, which is flat, and level with surface. Tumour on thigh near the trochanter is gone, and nothing remains to mark its former site. For the first time it is noted that the thyroid gland is slightly enlarged.

February 8th.—Had herpes facialis last week, most marked about the corners of the mouth, but it is now fading

rapidly. Says he has had herpetic eruptions on face several times during the past two years. Arsenic, iron, and bismuth administered regularly.

9th.—No nervous paroxysms lately, and has been walking about the ward. Hair of scalp is thinning from constant scratching, and the skin of scalp is redder than formerly. The back, between the shoulders, and the chest at root of neck, are scaly from scratching. Abdomen less dark than formerly. All the tumours have disappeared from the trunk except one just above the left nipple, one three inches to the left of right nipple, and one in right axilla, making a reduction from forty to four in six months. The largest tumour now on the trunk is not larger than a split cherry. No cicatrices have been left, and only three tumours are followed by pigmentation. For the intense itching patient has used strong ointments of carbolic acid before coming under my care, and without good results; so a salve containing a drachm of dilute hydrocyanic acid and an ounce of vaseline is ordered, with the hope of diminishing friction. Bismuth discontinued.

28th.—Walking causes feet to swell, so horizontal position is ordered. Bowels have been loose again, and patient has been taking only bismuth for past week; and to-day three drops of Fowler's solution are added to the dose. Many tumours on the extremities have increased in size. It seems that whenever the arsenic is stopped the tumours begin to grow, and discharge more profusely. It is also a queer fact, first noticed by the patient himself, that whenever single tumours enlarge and discharge, the smaller ones in their vicinity diminish or disappear.

March 1st.—Has had two bloody stools, accompanied by an odour similar to that of the feet, and very offensive. Rectum feels very sore. The small toe of left foot is ulcerating and quite painful, so a mixture of iodoform, bismuth, and starch is applied. General health remains about the same. Bowels have been moving twice a week.

10th.—The aspect of the extremities has changed a great deal; four new tumours have come, and old ones disappeared. In the evolution of these growths, there is never any loss of tissue. The smaller ones disappear by absorption, leaving

a bluish-red mark level with the skin. This in turn disappears, leaving a temporary pigmentation. The larger growths usually become moist and raw in appearance, discharge an ichorous pus for a while, then become dry, contract, and disappear. In accomplishing this last process it is not uncommon to see a long tumour with narrow neck contract to a spheroidal shape, and rest in a sort of crater of raised skin. Attached to the centre of this crater by a narrow pedicle, it rests there like a ball in a socket, and can easily, though not without producing pain, be detached from its cup. The right arm and forearm now present five tumours for inspection, the largest of which is the size of a pecan-nut; while on the left arm and forearm are seen fourteen of these growths, the largest of which is the size of a split cherry. There are no tumours on the back of the hands, and only two or three indurated spots indicate the site of former tumours of the palms. None of the first phalanges are diseased, and the first two fingers of the left hand are unaffected. Flexion of the fingers is performed now with ease, and the deep red colour of former disease now exists only at the edges of the nails. Both hands are swollen, but the left is better than the right. Seven tumours can be counted on the left lower limb near or about the knee, and ten on the right in the same locality. These are irregularly distributed above and below the joint, being for the most part on its lateral borders. They are larger than those of the upper extremity, several being the size of pecan-nuts, only somewhat flatter. They are not unlike hæmorrhoids in appearance.

Pigmentation and roughness of thighs and upper half of legs remain as before. Toes are smaller and have lost the appearance of a continuous mass of tissue, and their divisions can be distinctly seen. Feet are swollen and œdematous, and have no tumours on dorsal surfaces. Not so with the lateral and plantar surfaces, for the right foot presents six moist, tender, pedunculated tumours, about the size of a large cherry, growing from its outer side. Under both feet are numerous prominent and slightly pedunculated tumours, which are largest at the heels, and prevent the patient from taking his wonted exercise about the ward.

Hydrocyanic acid salve is still used to lubricate the skin, though its effect on the pruritus is very slight.

18th.—Bismuth to be omitted, as bowels have not worked for six days. Has not taken iron for one month. Resumes to-day the iron and arsenic mixture, taking five drops of the Fowler's solution at a dose. Fingers are swollen, and ichthyol replaced by iodoform salve.

April 5th.—A swelling the size of a hen's egg divided in half longitudinally has been present several days on the left arm, just in front of and above the enlarged epitrochlear gland. It is very tender to the touch, and gives pain; but the skin above it is not inflamed. Corresponding to this on the right arm is a tender nodule which has been present only a few hours. Patient states that he had a number of similar painful spots, with swelling along the course of the saphenous vein in the thigh, about a year ago, and confidently asserts that these will soon pass away as did the others.

11th.—No new tumours have appeared, and all old ones are smaller except a fungoid growth the size of a walnut on the left arm. The trunk and thighs are covered with a smooth, reddish, indistinct, macular eruption, resembling secondary syphilitic manifestations. These macules are about the size of a silver dime, or smaller. Bowels have been loose again, but have been checked with bismuth. Rectum and anus are tender, but no new growths are found. Swelling and tenderness of arms above the elbows have greatly diminished. Complains of a burning sensation in meatus urinarius when he passes water. The glans penis, though not swollen, is red and tender, and the meatus a little puffed, as in acute gonorrhœa. Urine remains normal, the specific gravity being 1019.

28th.—A careful examination to-day discloses the following:—Condition of face just as formerly, only the skin is thicker and more permanently red. The macules on the trunk are not so numerous, but the skin remains pigmented. There are many excoriations produced by scratching. *Not a single tumour can be found upon the trunk.* On the right arm are counted three tumours, all about the size of a pea. On the left arm are likewise three tumours, two of which

are the size of a pea; while the third is the size and shape of a silver dollar, only twice as thick, and attached to the skin by a short pedicle which passes to its centre, and has the thickness of a lead pencil. The tender new growths just above the elbows give no more pain, and are now the size of the enlarged epitrochlear glands already noted. These are now regarded as lymphatic glands which were formerly too small to be felt, but which have enlarged with irritation. Both forearms remain pigmented and rough: on the left are two small tumours; the right is free from them. Both hands are somewhat œdematous and swollen, and the left more so than the right. There is a decided improvement in the hands, though the thickened skin remains; and small, fungous swellings are still found on the thumbs and little finger, more particularly on the left hand, which was the better of the two some six months ago. Projecting from the gluteo-femoral sulcus on the right side is a tumour the size of a large chestnut. This is dry and in a process of resolution, as are also two pea-sized tumours on the right thigh. The prominent tumours noted upon the knees a month ago have diminished in size and number, for the right knee has but three small nodes, while the left has two pedunculated tumours, size of a filbert, projecting from the prominences made by the head of the fibula and internal tuberosity of the tibia. Both legs are œdematous, shiny, and red, but not painful; and on them can be found but one tumour. This is the size of a pea, and situated in the lower half of left leg. It is now recalled that, several months ago, a large discharging tumour which was just above the right ankle, and which gave considerable discomfort, has disappeared, leaving nothing but a slight redness of the skin. The feet, though never as well as now, still show the worst phase of the disease. The tumours occur about the prominences only, though the skin of the instep above and below is red and tender. The toes of both feet are equally affected, and can now be moved separately by the patient. The right heel is in good order, but attached to the left are five fungoid masses, each about the size of a filbert, discharging a watery fluid. The adenopathies remain about the same.

*Remarks.*

Such is the clinical history of this interesting case during a period of eight months. It would be interesting to compare it with other cases which do not exactly conform to the characters of the fungoid mycosis of Alibert, reported by Tilbury Fox,[1] Van Harlingen,[2] Hardaway,[3] and Hyde,[4] and with which cases the one here recorded has many symptoms in common. But space forbids. When the man came under observation he was weak and emaciated, and though he cannot be fairly said to have gained in weight, he has not lost; and if not stronger, he is no weaker now than then. That arsenic has been useful in the treatment I do not doubt, for the tumours have become worse whenever this was discontinued, even for brief periods. On the other hand, we find that the patient has taken this medicine with few intermissions for eight months, and during this period the tumours have all diminished in size, while many have disappeared entirely. As the notes show, iron was frequently combined with the arsenic, and has doubtless proved itself useful. We know also that ichthyol was useful as a local application, for it was continued on the hands, and there only, often when the arsenic was stopped; and while new tumours appeared elsewhere the hands steadily improved. The persistent pruritus remains unabated, and it is possible that the arsenic may have aggravated it, or at least impeded its improvement. It will be noticed that the nervous paroxysms and fevers referred to in early notes gradually ceased, and that the patient has not been harassed with them for some time.

Freshly drawn blood has been recently examined in the ward by my friend Dr. A. McShane, who used the hæmocytometer of Gowers. The doctor found in a cubic millimetre of blood 4,680,000 red corpuscles and 36,000 white cor-

[1] Fibroma Fungoides, 'Skin Diseases,' 2nd Amer. ed., New York, 1873.

[2] Ulcerative scrofuloderm, 'Arch. of Derm.,' April, 1879.

[3] Multiple tumours of the skin, accompanied by intense pruritus, 'Arch. of Derm.,' April, 1880.

[4] Myeloma cutis, 'Diseases of the Skin,' 1883. The author has just received the second ed. of Dr. Hyde's work, in which he refers to the same case as one of mycosis fungoides.

puscles, and remarks, "The ratio of white corpuscles to the red is thus 1 to 130, which ratio is much greater than that observable in health." Now when we consider that the usual proportion is 1 white to 350—500 red, we see that there are at least three times as many leucocytes in the blood as there should be in health. There seems to be no very marked diminution of red cells.

*Examination of Tissues.*

For microscopical study tumours were removed from the patient at three different times, and sent to the pathological department of the hospital. The first specimen, already referred to, was stained for leprosy bacilli, and none found after the examination of many sections. A second, the size of a cherry, was removed November 22nd, and a third about six weeks later. The last specimen was the smallest focus of disease that could be found, and was the size of a small pea, having healthy tissue attached, and included the whole thickness of the skin.

These were all sent fresh to Dr. H. D. Schmidt, the distinguished pathologist of Charity Hospital, New Orleans, who has studied them carefully, and, after much labour, has submitted to me the following report, with drawings from his own skilful and accurate pen:

"The tumour first sent to me for examination had been taken from the side of the patient just over the liver, and from my microscopical examination of thin stained sections of it I was rather inclined to regard it sarcomatous in its nature. Being unable to discover in the sections any trace of a reticulated adenoid tissue, mentioned by some authors, and to which you particularly directed my attention, I suggested to you to remove from the body of the patient one of the smaller tumours of recent growth, on which we might possibly observe the histological development of the neoplasm. What I had suspected proved true, for the sections made of this second and smaller tumour which you removed from the arm of the patient, though not showing the very first stage of the disease, exhibited, nevertheless, the true

structure and development of the growth to full satisfaction. As will be seen directly, there was some difference observed in the structure of the two tumours, though they were derived from the same patient—a phenomenon which, however, admits of a satisfactory explanation. Although the larger tumour, taken from the side of the patient, was the first examined and studied, I shall commence my description of the nature and development of this neoplastic growth with the smaller and last specimen taken from the arm of the patient.

"To illustrate the subject, and to render its description more perspicuous to the reader, I have carefully made from the microscope a number of drawings representing the different phases of development of the tumours of mycosis fungoides; they will accompany this report.

"In turning now our attention to Fig. 1, which represents a section of the smaller and younger growth, magnified about 40 diameters, we notice at *a* the so-called horny layer (stratum corneum), at *b* the layer of the prickle-cells, or mucous layer (rete or stratum mucosum) of the epidermis, and at *c* the papillary layer (pars papillaris) of the corium. In the latter we notice a number of well-defined round spaces, or areolæ, *d*. These spaces are also met with in the pars reticularis of the corium, where they represent the areolæ, or lymph-spaces, situated between the bundles of connective tissue of this part of the skin from which the radicles of the lymphatic vessels take their origin. These spaces, which differ considerably in diameter, increase in size during the development of the tumour. In some instances, even, a number of the lymph-spaces fuse with or coalesce into one another (Fig. 1, *e*), forming, surrounded by a sort of a capsule of hyperplastic connective-tissue bundles (*f*), a compact mass, which, as may be observed in this figure, constitutes the greater part of the whole tumour.

"Let us now trace the mode of development of this neoplasm by referring to Fig. 2, which represents a small portion of the tumour seen in Fig. 1, including the epidermis and a small part of the corium, magnified about 250 diameters. Leaving the strata of the epidermis to a later consideration, we shall first direct our attention to a number

of small round cells (so-called leucocytes or lymph-cells) observed between the bundles of connective tissue of the papillary and the adjacent reticular layers of the corium. In the drawing (Fig. 2) before us these cells do not appear very numerous, for the reason that this specimen of the neoplasm did not represent its very first stage of development. But judging from my own observation, and from the statements of other pathologists, I may safely presume that these small cells are the first pathological elements appearing in the history of the neoplasm under consideration, giving rise to the subsequent pathological changes in the corium of the invaded part of the skin. Though not represented in my drawing (Fig. 2), I have observed two nuclei in a number of these cells, and also, in many instances, two of the cells lying very close to one another, thus showing that their multiplication takes place by the mode of division. As regards their origin, it will, of course, be difficult to determine whether they are derived from the blood or lymph, or from the normal connective-tissue cells.

"Throughout both the papillary and reticular layers of the corium will be observed a number of smaller or larger elliptoidal spaces closely packed with small cells (Fig. 2, *e*), which cells have become polygonal in shape by mutual pressure. These cell-nests, as they may properly be called, have very probably been formed by the multiplication of one or even more of those individual cells met with between the connective-tissue bundles. In the loose tissue of the pars reticularis (Fig. 1, *f*, and Fig. 2, *h*) these cells, when increasing in number, simply fill up some of the small oblong interspaces of the loosely arranged connective-tissue bundles, whilst in the denser tissue of the pars papillaris (Fig. 1, *c*, and Fig. 2, *d*) the small elliptoidal spaces are formed by the cells, which, during their increase in number, press asunder the parallel and closely arranged connective-tissue bundles. At any rate, in both instances the cells gradually assume a more multipolar form, from which filiform processes are growing out, which, by growing toward and fusing with those of neighbouring cells, eventually form a sort of reticulated so-called adenoid tissue (Fig. 2, *f*) mentioned by some of the authors in their description of the

pathological anatomy of these tumours. The final conversion of the small round lymph-cells into adenoid tissue, however, does not only take place in the cell-nests, but also in those single individual cells distributed throughout the connective tissue of the papillary and reticular layers of the corium (Fig. 2, *d* and *h*), where they may be observed to assume also, as in the case of the cell-nests, a multipolar form; while the filiform processes, proceeding from neighbouring cells, likewise unite to form an imperfect reticulum throughout the connective tissue.

"The adenoid networks above described, formed both from the cell-nests and from those single cells distributed throughout the connective tissue, consist of fine fibrillæ connecting the individual multipolar or stellated cells with one another. There are, however, other so-called lymphoid networks observed in this tumour, which consist of more or less *coarse* connective-tissue fibres, and contain, besides a very small number of multipolar cells, also a number of single nuclei. These networks (Fig. 1, *e*) appear to be derived from the endothelial cells lining the round and larger lymph-spaces of the connective tissue of the pars reticularis. From the protoplasm of these cells also, as in the case of the cell-nests above described, processes grow out, which by meeting and uniting with the processes of neighbouring cells form the reticulum, which here, however, consists of more or less thick and heavy bundles of connective-tissue fibres and comparatively small meshes (Fig. 3, *a*). In the coarse bundles of this reticulum a number of small single nuclei are observed, which represent the remains of the nuclei of the original multipolar cells, the whole protoplasm of the latter having been used up in the formation of the fibres of the reticulum. Only here and there some of the original multipolar cells are still observed in the meshes of the reticulum, as seen magnified about 250 diameters in Fig. 3, *c*.

"In referring again to Fig. 1, which represents a section of the whole small and more recent tumour, there will be observed a considerable number of these coarse reticula (*e*) just described. They are enclosed in a sort of a capsule, formed by coarse bundles of hyperplastic connective tissue of the pars reticularis (*f*), from which processes are seen to

arise and proceed into the interior of the whole mass, forming septa (Fig. 3, *b*) between the original reticula. The latter, circumscribed by the capsule, form almost the greater part of the whole tumour.

"Some of the spaces, filled with multipolar cells united by the fibrillæ of their processes, are also observed at the borders of the papillary layer, as represented in Fig. 2, *g*, and Fig. 1, *d*. These spaces are likewise, as it appears, original lymph-spaces, and the cells which they contain may possibly be derived from the endothelial cells lining these spaces; though, on the whole, it may be said that it is very difficult to determine the true origin of these cells.

"In reviewing the process of the formation of the adenoid network from the cell-nests, such as I have described it above, a certain obscure point relating to this process will be noticed to still remain unexplained; this point involves the question, in what manner can the interspaces or meshes observed between the fine fibrillar processes of the multipolar cells, and forming the adenoid network (Fig. 2, *f* and *g*), be formed from a *closely packed* mass of cells as seen at *e*? The only plausible explanation which I find to meet this question is, that the multipolar cells, while they give rise to their filiform processes, secrete a fluid which, by gradually distending the space or wall of the cell-nest, makes room for the growing processes and their filaments, which room or space becomes eventually identical with the meshes of the network.

"As regards the connective tissue of the corium, it is found to be in a hyperplastic condition, indicated particularly by the coarse bundles of connective-tissue fibres of the pars reticularis (Fig. 1, *f*, and Fig. 3, *b*), as well as by the deformity or even complete disappearance of the papillæ by the hyperplasia of the connective tissue of the pars papillaris (Fig. 1, *c*, and Fig. 2, *d*).

"In passing now from the consideration of the corium to that of the epidermis of the tumour in question (Fig. 2, *a*, *b*, and *c*), it may be stated that here the mucous and granular layers, as well as the septum lucidum, showed no abnormal changes; whilst the horny layer, besides having diminished in thickness, presented a peculiar appearance,

namely, the walls of its component cells, instead of being marked by a fine double contour, appeared in this case to be composed of several superposed layers, indicated by several lines, as may be observed in Fig. 2, *a*. In examining the drawing more closely, however, it will be observed that these lines do not correspond to the outlines of the individual cells, as they should in representing the outlines of individual layers, or deposits, upon the interior of the cell walls; but that, on the contrary, the greater number of these lines pass from one cell to a neighbouring one, either in a parallel or oblique direction. For the latter reason it appears to me more probable that the supernumerous lines of this cell wall indicate the walls of *collapsed* cells—a phenomenon which at the same time would satisfactorily account for the decrease in thickness of the horny layer.

"Having thus far treated of the structure and development of the smaller and more recent tumour, which you took from the arm of your case of mycosis fungoides, let us pass to the consideration of the structure of the tumour which I first examined, and which you took from the side of the patient just over the region of the liver. In doing so we shall refer to Fig. 4, which represents a small portion of the irregular surface of this tumour, magnified about forty diameters.

"At the first glance upon this drawing we must notice the considerable deformity of the layers of the epidermis caused by the abnormal growth of the corium. As in the younger tumour above described, we likewise find here the horny layer (*a*) of the epidermis reduced in thickness. The mucous layer (stratum mucosum, *b* and *c*), also, is found deformed by the abnormal growth of the papillæ (*c*), as well as by the rest of the corium (*d*). Although this tumour was larger, and represented an older growth than the one described above, its microscopical examination and study showed the absence of any formation of lymphoid so-called adenoid tissue, the principal pathological changes simply consisting in the production of very numerous cells, and, besides some spindle-celled sarcomatous stroma, a hyperplasia of the connective tissue of the corium, indicating a lower grade of organisation than met with in the smaller tumour above described.

In referring again to Fig. 4, *d*, which represents the corium of the tumour, the cells will be observed arranged in larger or smaller groups, which, on their part, are arranged in rows; they are embedded in the hyperplastic connective tissue. Most of the empty spaces observed in this part of the tumour represent the sections of blood-vessels, while others may represent sections of lymph-spaces.

If we now examine Fig. 5, representing a small portion of corium, as exhibited in Fig. *d*, magnified about 250 diameters, one part of these cells will be found lining sections of lymph-spaces (*a*), while the other part is embedded in the hyperplastic connective tissue (*d*). At the same time a slight difference may be observed in the comparative shape and size of these cells; for whilst those in the lymph-spaces exhibit a somewhat irregular form, resembling the endothelial cells of vessels, the other, placed between the fibrous bundles of the connective tissue, are somewhat smaller in size and more spindle-shaped. Judging from the small groups (*b*), in which the cells are placed closely to one another, their multiplication must take place by the mode of division. In this drawing, also, a number of empty spaces (*c*) are met with, which here very probably represent sections of lymph-spaces.

From what I have already said above, it may, then, be presumed that the cells met with in this tumour are derived from the endothelial cells lining the areolæ or lymph-spaces of the connective tissue, as well as from the small cells placed between the fibrous bundles of this tissue itself. But in referring again to Fig. 4, and in carefully examining the greatly deformed remains of the papillæ, as shown in this drawing at *c*, a number of rows, formed by groups of cells, will also be observed in this part of the tumour. And it will furthermore be noted that these rows correspond in their arrangement to that of the blood-vessels of the normal papillæ of the corium, for which reason I am much inclined to regard these latter cells as having been derived from the cells contained in the walls of the blood-vessels. A part of the cells met with in the pars reticularis may have originated in the same manner; this postulate appears to me justified,

as I have failed to discover any minute blood-vessels in the sections of this tumour.

Although throughout the greater part of this tumour the groups or nests of cells appeared to be embedded in a hyperplastic connective tissue, as represented in Fig. 5, there were, nevertheless, a number of places met with, particularly in the deformed papillæ, in which a stroma, consisting of minute spindle-shaped cells, could be distinguished, and in which, besides, the whole mutual arrangement and character of all the histological elements of the growth pointed to the character of sarcoma, which observation, during my first examination of this tumour, had inclined me to regard the whole growth as sarcomatous in its nature.

As regards the epidermis of this tumour, it may be stated that whilst its horny layer was greatly reduced in thickness, and exhibited the same changes in the walls of its cells, already described in connection with the smaller and younger tumour, the stratum mucosum appeared, though deformed in its general shape, to have undergone but very slight changes in its histological character.

In reviewing the descriptions of the structure and development of the two tumours taken from one and the same patient, though from different parts of his body, a difference in the character and arrangement of the histological elements of the tumours, as well as in the general construction of the latter, will be found to exist. At first sight this difference appears so striking that, without the knowledge of both tumours having been developed upon the same patient, the pathologist, in studying the character of these tumours, might very easily be led astray, and regard them as distinctly different in their structure, and as being derived from two different patients. In knowing, however, that these tumours have in reality been developed upon the same patient, and in studying and comparing their structures with one another a little more closely, it will be found that the two growths simply represent different stages of development. For whilst in the one the pathological process advances only to the formation of a great number of cells, appearing mostly in the form of groups or nests of cells—as well as, though only in some parts of the tumour, to the

production of a number of small spindle-shaped cells, representing, as already mentioned above, a sarcomatous stroma —we find in the other tumour the same production of cells, probably of the same origin, but endowed with a superior force of organisation, and in consequence developing into a higher kind of tissue, resembling in structure that met with in the lymphatic glands known as adenoid tissue. And it is this difference in the degree of development observed, as in the case under consideration, to exist in the tumours derived from different patients suffering from the same disease, and causing a different appearance of the structure of these growths, that has given rise to the discrepancy of opinion as regards the exact nature of the tumours and the disease in question, which has existed, and to a certain extent perhaps still exists among some pathologists.

Abstaining from making any special remarks as to the etiology of this peculiar affection, I will simply repeat that the first pathological change observed in the skin consists, very probably without regard as to their origin, in the appearance of very great numbers of small round cells. In the small tumour examined and studied by myself, this very first stage of the development of the neoplasm had, as I have already mentioned before, almost passed, though many of these small cells were still observed throughout the papillary layer of the corium, as seen in Fig. 2, *d*. But in examining Fig. 1 of the illustrations accompanying the statements of Dr. Longstreet, concerning his examinations of the tumours of Dr. Duhring's case of this disease ('Archives of Dermatology,' January, 1879), this stage, characterised by the appearance of great numbers of small lymph-cells in the corium, will be found represented.

As regards the adenoid networks which I have described above, I may state that it is only the one consisting of fine fibrillæ which I have thus far seen described and represented by a few authors in their writings on the subject; whilst the reticulum, consisting of those coarse bundles of fibres as represented in Fig. 3, I have as yet never seen mentioned or represented by drawing.

As to the etiology and exact nature of mycosis fungoides, I shall for the present likewise forbear from expressing any

positive opinion, and, in consequence, classification of this neoplastic growth, though I may simply say that thus far I am rather inclined to regard it as being in some way or other related to the lymphatic system. The designation "mycosis fungoides," at any rate, appears to me wrong. Ranvier's "lymphadème cutanée," though it may not be perfectly correct, nevertheless appears to express somewhat closer the true nature of the neoplasm than the above original designation.

In reviewing the history of this remarkable case, we find that without apparent cause the disease began as an eruption similar to, if not identical with eczema, accompanied by an intense pruritus which has continued to this day (May 12th, 1888).

The tumours, which later on formed a conspicuous feature of the disease, did not appear until after the frost-bite in January, 1887, or three and a half years after the beginning of cutaneous inflammation. The tumours have spared no portion of the body except the face and scalp, and occur on the thinnest as well as the thickest surfaces. Though tender to the touch they are not painful, and though congested they have never bled from ulceration.

Their occurrence on the hard palate, the external auditory meatus, the glans penis, and occasional tenderness within the rectum during defecation, with bleeding therefrom, go to show that the mucous membranes are by no means exempt from the disease. How far the mesenteric glands and internal organs are affected it is at present impossible to say.

The spontaneous appearance and disappearance of the tumours is an interesting and curious feature of the disease, for several that grew to the size of a pecan-nut were observed to pass through their stage of growth and resolution within six weeks, while certain others, half the size, would remain three times as long. In a general way it may be stated that the soft, discharging tumours grew largest and disappeared soonest.

Thus far the disease seems to be dermal rather than hypodermal, beginning in the skin and remaining there. It were hard to say how true this statement may be with re-

ference to the toes; but as the inflammation has not yet destroyed the deeper structure after months of disease, it can be understood how superficial the morbid process must be. The only subcutaneous inflammation noted has been that of the numerous enlarged lymphatics; and it is possible that the swelling mentioned as having occurred in the region of the saphenous vein in the thighs was also due to inflammation of the lymphatic glands distributed along the course of that vessel.

### *Conclusion.*

We see, then, in this disease an unusual involvement of the lymphatic glands, many of which, so small and insignificant in the normal state as not to be noticed in the majority of dissections, become irritated and swell to the size of a butter-bean, in one case attaining the size of a pigeon's egg. In addition to the clinical fact of slight but constant œdema of the extremities, the microscope discloses marked changes in the blood and tissues.

In the former we find a decided increase of white corpuscles; and in the latter an adenoid growth, accompanied by dilatation of the lymph-spaces of the skin, with a decided hyperplasia of their endothelial cells occurring early in the disease.

Now, admitting the possibility of earlier changes than those which took place in the lymph-spaces, such as a round-cell deposit in the connective tissue of the corium, and hyperplasia of the cells of the blood-vessel walls (which latter was observed, however, only in the older tumours), I am inclined to look upon this affection as a disease *sui generis*, which, in the light of the foregoing clinical and pathological observations, is to be considered as "in some way or other related to the lymphatic system."

## DESCRIPTION OF PLATE.

FIG. 1.—Section of the Entire Tubercle, taken from the Arm of the Patient; magnified about 40 diameters.

*a*. Stratum corneum. *b*. Stratum mucosum. *c*. Pars papillaris. *d*. Lymph-spaces of the corium, filled with stellated cells and their reticulum. *e*. Lymphoid network, consisting of coarse fibrous bundles. *f*. Hyperplastic connective-tissue bundles of the corium, forming a sort of a capsule around a part of the tumour, consisting of a number of the coarse reticula, and giving rise to numerous septa passing between the latter. *g*. Transversely and obliquely cut bundles of connective tissue of the corium. *h*. Subcutaneous connective tissue.

FIG. 2.—Small Portion of the Epidermis and Upper Part of the Corium of the Growth of Small Tumour represented in Fig. 1; magnified about 250 diameters.

*a*. Stratum corneum. *b*. Stratum mucosum. *c*. Stratum granulosum. *d*. Pars papillaris of the corium, containing small round and multipolar lymph-cells. *e*. Nests formed by these cells. *f*. Nests of which the cells have become multipolar, their processes uniting with one another to form the adenoid network of fine fibrillæ. *g*. Areolæ or lymph-spaces of the connective tissue of the corium, filled with stellated cells and their reticulum. *h*. Connective tissue of the pars reticularis, containing stellated cells with their network. *i*. Bundles of hyperplastic connective-tissue fibres of the pseudo-capsule, Fig. 1.

FIG. 3.—Small Portion of the Coarse Adenoid Reticula represented in Fig. 1; magnified about 250 diameters.

*a*. Coarse bundles of connective-tissue fibres of the reticulum. *b*. Bundles of hyperplastic connective tissue, derived from the pseudo-capsule, and forming septa between the adenoid reticula. *c*. Original multipolar cells that have not taken part in the formation of the reticulum, seen in the meshes of the latter. *d*. Small nuclei, representing the remains of the nuclei of the original multipolar cells from which the reticulum was formed.

FIG. 4.—A small portion of the Irregular Surface of the large Tumour; magnified about 40 diameters.

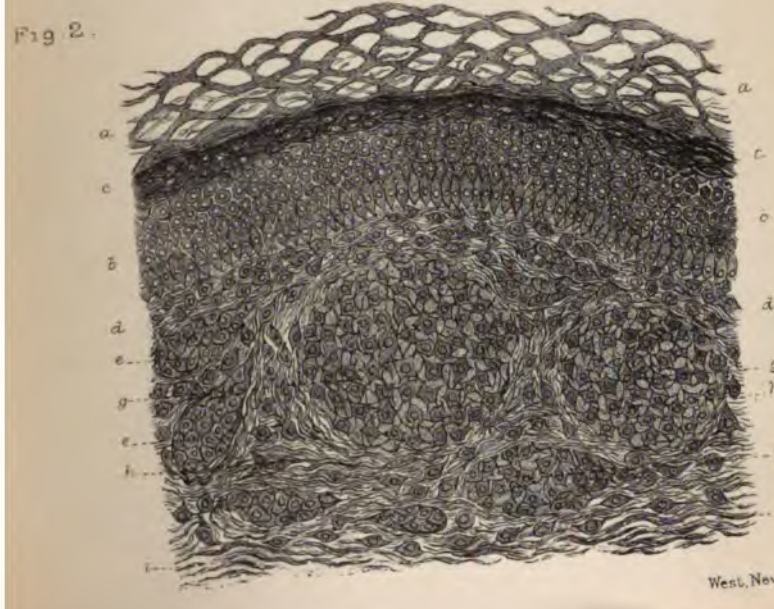
*aa*. Stratum corneum. *bb*. Stratum mucosum. *c*. Deformed papillæ of the pars papillaris, containing nests of neoplastic cells, probably derived from the cells in the walls of the blood-vessels. *d*. Corium, containing rows of neoplastic cell-nests.

FIG. 5.—Small portion of the Corium of the larger Tumour represented in Fig. 4; magnified about 250 diameters.

*a*. Sections of lymph-spaces, containing endothelial cells. *b*. Cell-nests, the cells of which have arisen from one cell, showing the multiplication of these cells taking place by the mode of division. *c*. Probable section of lymph-spaces. *d*. Hyperplastic connective tissue, containing smaller neoplastic cells, many of which are spindle-shaped.

Plate I.

Fig 2.




West, Newma

Plate II

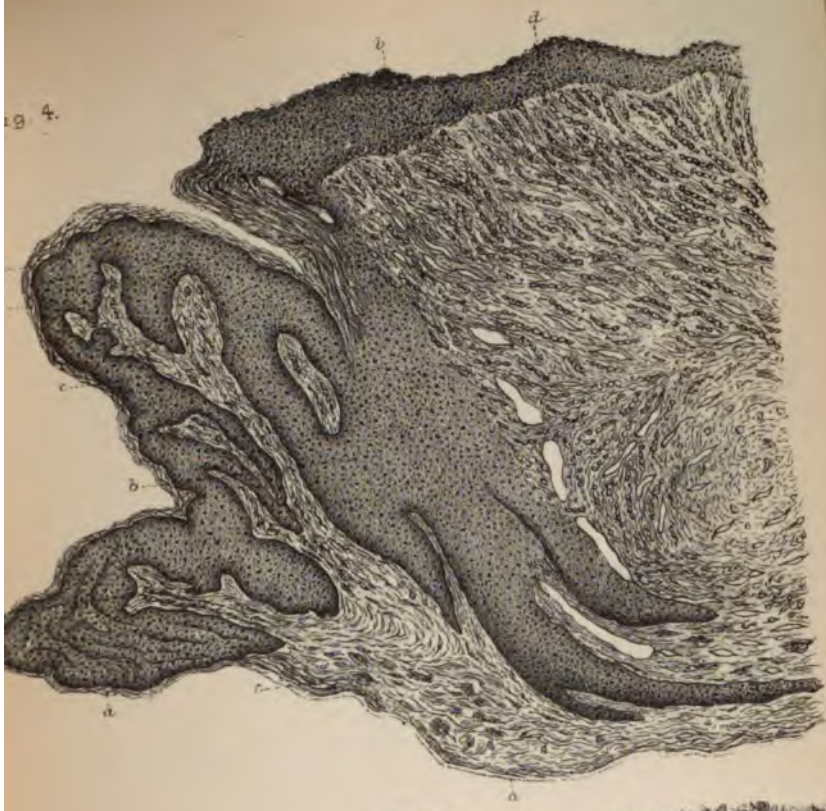
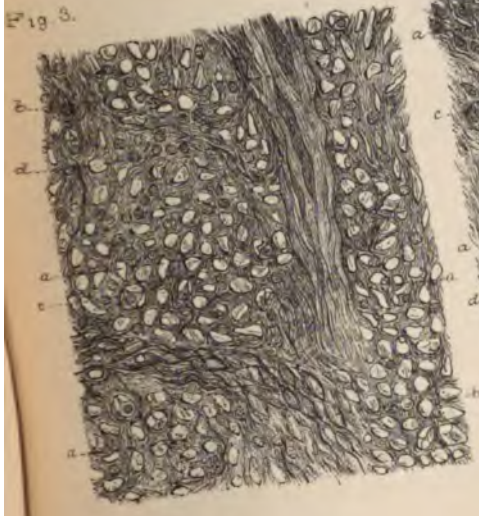



Fig. 5.

Fig. 3.




West, Newman lith.

# PELLAGRA.

BY

LUDWIG BERGER, M.D.,
IMPERIAL-ROYAL MEDICAL OFFICER FOR THE DISTRICT OF GRADISCA.

TRANSLATED AND ABRIDGED BY

FRANK H. BARENDT, M.D.Lond., F.R.C.S.Eng.

# PELLAGRA.[1]

PELLAGRA, derived from the Italian *pelle*, skin, and *agra*, rough, *Fr.* pellagre, *Sp.* rosa delle asturie, also known in Italy by the names of mal rosso, scorbuto alpino, and mal della miseria, is a disease of warm climates between 42° and 47° of latitude. It is mostly endemic, not contagious, runs a chronic, afebrile course, and usually attacks the poorer members of rural populations where maize is especially cultivated.

Pellagra occurs in Spain, Portugal, France, Italy, Roumania, Moldavia, Wallachia, in the island of Corfu, in Austrian Tyrol, and probably also in South Tyrol. It is said to occur sporadically in Algiers and Mexico. On the other hand, the British Isles, Germany, Russia, Scandinavia, Holland, Belgium, and Switzerland are quite free.

Pellagra appeared some fifty or sixty years after the introduction of maize from America, first in Spain, spreading to France, Lombardy, &c. Reliable statistical dates of its first appearance are completely wanting. The first trustworthy information about this disease came from Spain, where *Gaspar Casal*, already recognising it in 1735, first described it in 1750 under the name of "mal de la rosa."

*Frapolli*, of Milan, was the first to use the name Pellagra in 1771. According to him and other Italians, the disease was already known at the end of the sixteenth century by the name of Pellarella.

In 1881 there were 103,958 pellagrons in Italy. In the

[1] A paper read at a meeting of Imperial-Royal Medical Officers of the maritime districts in Volosca-Abazzia, September 28th, 1889.

writer's district of Gradisca (Austria, on the Italian frontier) in 1888 there were 790, or 1·2 per cent. of the population.

*Balardini* gives the following description of the disease. About the time of the vernal equinox, as the peasants are preparing the land for sowing, they often complain of unusual bodily weakness; although apparently in the best of strength, they are mentally depressed and altogether disinclined for work. Later on the backs of the hands and feet, and other regions exposed to the sun's rays, become shiny, tense, and display slight redness, gradually passing into lividity. The epidermis dries up by degrees, and is shed in the form of branny scales. This erythema, which usually spares the two terminal phalanges of the fingers, is not constant in persons who are not continuously exposed to the sun. In the autumn symptoms improve, and towards winter disappear completely; the patient is fairly well, and thinks no more about his trouble of the previous spring. The following spring, however, they recur, sometimes in an aggravated form, depending upon individual predisposition and the circumstances of life of the patient, run a similar course, but leave traces behind.

This is the *first* stage of pellagra, and generally lasts some time, during which the patient is alternately well or ailing.

In the course of events a marked decline in the bodily strength is noticeable. Symptoms increase in severity, and fresh ones make their appearance. The skin on the back of the hands becomes more livid, furrowed, chapped, and callous; the lips pale, the tongue bright red more or less fissured, and the salivary secretion is increased. Disinclination for food alternates with voracious appetite, and he complains of burning in the epigastrium, pyrosis, cardialgia, colic, and a tendency to diarrhœa. This, which is the *second* stage, is also accompanied by symptoms of nerve disturbance—sleeplessness, troubled dreams, frequent giddiness, heaviness, and oppression of the head. Later on supervene tremor of the lower extremities, with a tendency to fall backwards, forwards, or sidewards, and recurring convulsive tetanic attacks.

In the *third* stage delirium and mania (mania pellagrosa) often appear. The weakness of the extremities increases,

and often ends in paralysis. Diarrhœa becomes more frequent and colliquative in character, loss of strength rapidly increases, and deep uncontrollable melancholia overpowers the patient, who has no desire to live, shows suicidal tendencies, and often takes his life by hanging or drowning. If he is prevented, or does not succumb to any intercurrent affection, complete dementia terminates this sad disease. The duration of pellagra cannot be precisely determined; it usually extends over a period of ten to fifteen years.

The above symptoms are those generally seen, but they vary considerably.

The course is sometimes so chronic that it can scarcely be said to shorten life, at other times so rapid that a fatal issue takes place in a few years.

The majority of writers agree that pellagra is a disease of the nervous system occurring amongst the agricultural population of certain countries, characterised by chronicity, and especially by psychic, sensory, motor, and trophic symptoms, accompanied by gastro-enteric troubles and progressive decay. Although pellagra attacks the whole organism, the organs that chiefly suffer are—

1. The skin: with the various forms of erythema.

2. The alimentary canal: anorexia, bulimia, pyrosis, cardialgia, dyspepsia, and diarrhœa.

3. The cerebro-spinal system: giddiness, oppression of the head, tremor, spasm, general bodily weakness, terminating in muscular paralysis, and insanity, most usually melancholia.

Nationality and race apparently exert no influence over pellagra.

Although no period of life is exempt from its attacks, yet it most frequently occurs between thirty and fifty. Pellagra is more often met with in women; this may be referred to their diminished resistance to disease owing to lactation and indoor occupation in insanitary dwellings.

### Heredity.

Several important writers incidentally mention facts in favour of hereditary influence. It is certain that the chil-

dren of pellagrous patients inherit a weakened nervous system, just as those of dipsomaniacs are more liable to neuroses. Still, hereditary influence in the strict sense of the term, as separable from other factors in the etiology of the disease, cannot be assumed as a factor.

### Contagiousness.

Contagiousness, which was only maintained by early observers, appears, according to *Hirsch*, to be excluded by the almost absolute immunity of pellagra which the urban population enjoys in spite of constant intercourse with the rural. Moreover the fact that the attendants on such patients, and those living in pellagrous districts, but using different food, remain perfectly free from the disease, as well as the circumstance that those not too far advanced recover on change of diet, refute the theory of contagiousness.

### Pathological Anatomy.

From the results of a number of autopsies made by *Lombrosa* and others, the dura mater is frequently found thickened and adherent to the calvaria, the arachnoid and pia mater are also often thickened, and subpial ecchymoses may be frequently noticed. Œdema of the brain substance and atrophy of the cortex are likewise present. *A. Verga* found in many cases superficial softening of the cerebellum and injection of the spinal meninges. The spinal cord is usually soft and pale. *Tonini* observed diminution of pigment in the nerve-centres, and fatty and occasionally calcareous degeneration of the tunica adventitia of the small blood-vessels. Diminution of pigment has also been noticed in the cells of the sympathetic and spinal ganglia. These changes may be regarded as atrophic in nature.

The heart is usually small, dry, and friable. The fibres are in a state of brown induration; fatty degeneration is seldom observed. The stomach is dilated, the mucosa pale and covered with abundant mucus. The muscular coat of the bowel is always thinned and pale. Liver and spleen

frequently atrophied. The kidneys are usually cirrhotic, but seldom show fatty degeneration. Muscles atrophied. The bones and especially ribs are very brittle. In the skin, sclerosis of the blood-vessels, papillæ, and the corium, as well as atrophy of the horny layer, are present. *Déjérine* found neuritis parenchymatosa of the nerves of the skin, especially on the back of the hand.

The most prominent post-mortem appearances are, as a rule, general diminution of pigment in the nerve-centres, and brown atrophy of the heart. However, no certain conclusion as to the nature of the disease can be drawn from the above morbid signs, as they occur in those who have died from marasmus or mental disease.

## Etiology.

The causes to which pellagra has been attributed are numerous, *e. g.* isolation, geographical situation, character of the soil, air, and water, uncleanliness, bad hygienic surroundings, with all their consequences, &c. We must, however, agree with Lusana's objection that all these conditions existed long before the appearance of pellagra.

It is a historical fact that the disease appeared after the introduction of maize, and universal observation shows that where this endemic affection occurs it has followed the abundant use of maize, and where it is not cultivated or used pellagra is absent, or at least not endemic. Consequently this circumstance supports the supposition, if it does not establish the fact, that pellagra is due to the use of this cereal.

## Theory of Pellagra.

Two theories at present prevail, both supported by eminent authorities, neither of which, however, can at present be accepted *in toto*.

The one represents pellagra as the result of insufficient nourishment, pure and simple; the other as the result of chronic poisoning from diseased maize.

The former may be termed, shortly, "the inanition theory,"

and is supported by *Billod, Gintrac, Lusana, Bonfigli*; the latter, or "intoxication theory," is held by *Roussel, Balardini, Lombroso, Cuboni, Neusser, Paltauf*, &c.

Pa. The supporters of the inanition theory adduce the following considerations:—They maintain that maize in itself is insufficiently nutritious; that in many places it never fully ripens; that it is very liable to disease, and consequently to have its nutritive value still further diminished; and lastly, that it is difficult of assimilation.

In spite of the statement that cases of pellagra may occur in districts where maize is not consumed, still it is pretty generally admitted that the affection results from its use.

The adherents of the maize theory have termed these rare sporadic cases of "pellagra without maize" pseudo-pellagra, and explain them as diagnostic errors; for similar erythemata have been observed among alcoholics and the insane, more especially in general paralytics.

*Bazin* and *Bouchard* are certain that in *Billod's* clinic, cases of herpes tonsurans and of herpes circinatus have often been mistaken for pellagra; and *Michelacci* states he has seen in hospitals epilepsy, malarial cachexia, and delirium tremens qualified as "pellagra." Pellagra only occurs endemically and extensively in those regions where maize is used almost exclusively as an article of diet.

The equally incontrovertible statement that there are countries where, although maize is very largely consumed, pellagra does not exist, clearly shows that maize alone is not the cause of the disease, but that, under certain conditions, it acquires pellagrogenous properties.

The view of supporters of the "inanition theory," viz. that the exclusive or preponderating use of maize as an article of diet causes pellagra on account of the small amount of nitrogenous element, has been proved by *Hirsch* to be quite untenable.

I. Although, no doubt, insufficient nourishment does induce symptoms of chronic starvation and marasmus, it never causes the characteristic features of pellagra.

II. Pellagrous patients are, in the early stages of the disease, by no means rarely, well nourished, and only begin

to lose flesh to any extent when other organs are implicated, especially the alimentary tract.

III. Numerous populations which live exclusively on rice or potatoes, which are much inferior to maize in the scale of nutrition, are quite pellagra-free.

Moreover the chemist *Dumas* declares, as the result of his investigations, that maize is an excellent nutritive food-stuff, both for man and animals. Hence, if a causal relation subsists between the use of maize and the origin of pellagra, it must be due to certain unnatural properties of the grain which it acquires under certain conditions, *e. g.* when damaged or diseased; and this brings us to the grounds on which the intoxication theory exists.

B. *Balardini* was the first to pay attention to fungi occurring in maize and their relation to pellagra.

At first he attributed the source of the mischief to the so-called *Sporisorium maidis;* but as the distribution of this fungus was not equally co-extensive with pellagra, he considered *Penicillium glaucum* (green mould), which is of much more frequent occurrence, to be the cause.

The harmfulness of *Penicillium glaucum*, however, was very soon excluded, as it is found where pellagra does not exist, and is a constant accompaniment of decaying albuminous matter. Similarly, it could not be demonstrated that *Ustilago maidis* (maize-smut) and *Sclerotium maidis* (maize-ergot) exerted any influence.

*Lombroso* now expounded the theory that the fungus itself was not the noxious element, but that a toxic principle, the product of fermentation in the parenchyma of the maize-grain during the growth of the *Penicillium glaucum*, was the *causa vera* of pellagra.

*Lombroso*, *Balardini*, and *Erba* undertook experiments to test the validity of this hypothesis. They fed fowls on diseased maize, they lost their feathers, became thin and paretic, showing nerve-symptoms ending in death. Human beings experienced burning in the throat, digestive disturbance, and diarrhœa.

*Lombroso* prepared a tincture of artificially fermented maize which produced, in healthy individuals, various intestinal and nervous symptoms. He also, together with *Erba*,

obtained an active oily substance which he termed maize oil, besides an extract, "pellagrozein." Even a watery extract of the residue, after previous exhaustion with alcohol, was to some extent active.

*Husemann* found in diseased maize a narcotic tetanic poison, and *Selim* demonstrated the presence of acrolein ammonia. As similar alkaloidal substances can be demonstrated in other kinds of grain, these researches, although valuable, are not conclusive.

As a result of bacteriological investigation, *Cuboni* attributes the poisonous effects to the *Bacterium maidis*, which is extensively met with in sea-damaged maize; as any other organism, according to him, does not produce any important change with the usual methods of storing. This bacterium develops only in imperfectly ripe or improperly dried maize, and even resists a temperature of 100° C. This fact accounts for maize flour not keeping so well as that of other cereals, and why maize bread so soon spoils. *Cuboni* maintains that this organism produces a true intestinal mycosis, which in turn reflexly causes various phenomena—as, for instance, in the case with worms. *Neusser* considers pellagra the result of intestinal auto-infection. *Paltauf* and *Heider*, of Vienna, in 1887, undertook thoroughly to investigate diseased maize chemically, microscopically, and bacteriologically. They conducted numerous culture and feeding experiments, and studied carefully the *bacillus maidis* of *Cuboni* and its relation to pellagra. Their conclusions are as follows:

1. Pellagra is not a mycotic parasitic disease.

2. It is not in *Cuboni's* sense an intestinal mycosis, *i. e.* that a certain bacillus (*B. maidis*) occurring in diseased maize inhabits the alimentary tract of pellagrous patients.

3. The organism belongs to the same genus as the widely spread potato bacilli.

4. In support of the view that pellagra is a chronic toxic affection—the result of the products of diseased maize—the bacillus maidis and bacillus mesentericus fuscus have been found to produce in maize-flour a toxic substance, the effect of which on white mice is narcotic and paralysing.

This substance may be extracted from diseased maize by

means of alcohol, and thus confirms Neusser's statement that the spirit from diseased maize may produce pellagra even in those who never use maize.

The adherents of the intoxication theory also bring forward the following statements:

1. The analogy of diseases arising from other diseased cereals, *e. g.* ergotism, acrodynia, as well as from diseased meat-ptomaine poisoning.

2. The complete immunity those enjoy who use sound grain only.

3. The isolation of poisonous substances from diseased maize, *e. g.* acrolein-ammonia of Selmi, the maizin of Husemann, and the pellagrozein of Lombroso.

4. The results of experiments with these substances upon man and animals.

The solution of the etiology of pellagra has not only a theoretic value, as many writers maintain, but is of the greatest importance to the whole question of the disease. For on the inanition theory the affection would be very difficult to cope with, as we are confronted with social conditions admitting of but slight amelioration. On the other hand, the intoxication theory offers a more favorable prospect for the eradication of pellagra.

## Prognosis.

This depends upon the course of the disease. In the first stage of pellagra it is very favorable, in the second much less so, and in the third absolutely unfavorable.

## Treatment.

As always happens with a disease difficult to cure, an endless number of remedies have been recommended. It is waste of time to enumerate them: antiscorbutics, acids, alkalies, sulphur, iron, and quinine have all had their advocates. Astringents and opiates are employed in the attacks of diarrhœa, warm baths, cold affusion, blistering in the

nervous symptoms. Lukewarm baths, with or without sulphur, have been particularly extolled.

*Lombroso* recommended paullinia (guarana) and calomel in profuse diarrhœa with nerve symptoms, acetate of lead in old pellagrous patients with joint pains, and considers arsenic a sovereign remedy from its antiseptic and antifermentative properties, having achieved very favorable results even without any change in the habits of life of the patient.

Theobaldi obtained good results with alcohol 30 grms. (f. ℥j¼) daily, and decoction of cinchona.

Transfusion of blood has been used without any material benefit. Every writer, however, agrees that only by strict regimen and complete abstinence from sea-damaged, and even from sound maize when this forms exclusively the food of the patient, a favorable issue may result.

## Prophylaxis.

According to the difficult views of the etiology of pellagra, various preventive measures are recommended. All authorities, however, are unanimous that the condition of the agricultural class must be improved. The cultivation of maize in districts where it does not readily ripen on account of the moisture of the land (frequent inundations) and cannot be properly dried, should be replaced by that of other cereals, wheat, rye, and barley, pulse, potatoes, &c. The maize used in the production of alcohol and beer may be employed as cattle fodder instead.

The trade in sea-damaged maize should be prohibited under severe penalties.

Maize for human consumption should be completely dried before garnering, and with this object placed in proper drying chambers, and afterwards stored in warehouses thoroughly well ventilated and protected from moisture.

*Cuboni* gives the following ready method for distinguishing good from bad maize-flour. A sample is moistened and set aside in a temperature of 25° to 30° C. (77° to 86° F.); should a disagreeable odour be detected in the course of six or eight hours, the flour is unfit for use. With sound flour

is change does not occur until after the lapse of some enty-four to thirty-six hours.

Maize-flour should never be used alone for making bread ; eat-flour and the usual ingredients—salt and leaven—ould always be added.

The bread should be fresh daily, and in loaves of not more an 1 kilo. (about 2¼ lbs.) in weight ; it should be baked by oper bakers, and not left to the peasants.

*Lombroso* recommends the maize-grain to be boiled in ne water first, and then after thorough cleansing and dry-g to be ground. One of the most important steps in er years, and one that has received official sanction, is the ection of public bakehouses with drying chambers attached r the maize-grain. For not only is disease of the maize us prevented by the use of these drying chambers, but its similability is promoted owing to the conversion in part of e starch into dextrin.

Particular attention should be paid to the sanitation of e dwellings of the presents, and especially the source of eir water supply should be beyond any possible chance of ntamination.

Finally, asylums in the centres of the affected districts ould be established for the relief and proper care of the re advanced pellagrous patients.

# DRUG ERUPTIONS.

## A CLINICAL STUDY

OF THE

## IRRITANT EFFECTS OF DRUGS UPON THE SKIN.

BY

PRINCE A. MORROW, A.M., M.D.,

CLINICAL PROFESSOR OF VENEREAL DISEASES; FORMERLY CLINICAL LECTURER ON DERMATOLOGY IN THE UNIVERSITY OF THE CITY OF NEW YORK; CONSULTING SURGEON TO THE BELLEVUE OUTDOOR DEPARTMENT; SURGEON TO CHARITY HOSPITAL, DERMATOLOGICAL DIVISION; MEMBER OF THE AMERICAN DERMATOLOGICAL ASSOCIATION, ETC. ETC.

EDITED

FOR THE NEW SYDENHAM SOCIETY

BY

T. Colcott Fox, M.B.Lond., F.R.C.P.,

PHYSICIAN FOR DISEASES OF THE SKIN TO THE WESTMINSTER HOSPITAL AND TO THE SKIN DEPARTMENT OF THE PADDINGTON GREEN CHILDREN'S HOSPITAL; LATE PHYSICIAN, VICTORIA HOSPITAL FOR CHILDREN.

# PREFACE.

THE general proposition that the physician should be familiar with the effects of every drug that he employs in the treatment of disease is axiomatic. He should not only be acquainted with the drug's normal typical mode of action, but also with its abnormal or incidental effects, the more especially since, in the case of drugs as in the phenomena of every-day life, it is often the unexpected that happens.

The abnormal phases of drug action are comparatively an unexplored field. While it has long been known that eruptive disturbances of various kinds may result from the use of certain drugs, yet the number of drugs in common use capable of causing cutaneous disorders, the clinical appearances which they present, and the conditions which influence their development, are not sufficiently familiar to the profession.

The changes in the skin caused by drugs derive a special practical interest from the fact that they sometimes simulate very accurately the eruptive fevers and other idiopathic affections of the skin, and it is important that the physician should be able to differentiate the clinical features, and correctly interpret the pathological significance of phenomena so widely different in their mode of origin.

It is only within the last few years that this subject has received much attention from the profession. When the enormously large number of cases of drug eruptions which have been recently reported is contrasted with the comparatively few formerly recorded, it is evident that a prolific cause of cutaneous disorders long escaped recognition.

No doubt the reason that drug eruptions have been signalised so much more frequently within the last few years is attributable to the more exact methods of modern observation, the greater care and precision with which etiological factors are traced, and the recognition of the influence of numerous pathogenetic agencies which formerly were not suspected to be the originators of morbid changes in the skin. A mine of etiological agencies in the production of cutaneous disorders has been discovered, not only in the case of drugs, but also in the vaccine virus, mental emotions, traumatism, menstruation, septicæmia, pyæmia, glycosuria, &c.

It is not proposed in this work to study the cutaneous action of all drugs which have been accredited with the property of producing eruptive disturbances. The list is a long one, and embraces many agents which are not in common use, and a consideration of their dermatopathic effects would be lacking in practical value.

The relations which these cutaneous phenomena bear to the drug's physiological action and to conditions of individual susceptibility have not been definitely determined. In the present state of our knowledge a satisfactory solution of the problem is, perhaps, not possible. We know little definitely of the laws of drug action, and still less of the conditions which govern individual susceptibilities.

The author's object has been to collect from all available sources well-authenticated observations relating to every form of cutaneous disorder thus far recorded from the action of drugs. To these have been added numerous personal observations, some of which have been already published, and others appear now for the first time.

It is hoped that these results will prove of value to the general practitioner, not only in directing his attention to the large number of drugs in general use capable of causing eruptive phenomena, but in familiarising him with their clinical appearances, so that he may be enabled to recognise and refer them to their true cause when occurring in his own practice.

The author desires to acknowledge the invaluable assistance of his friend Dr. Charles Rice, who has furnished a

es of valuable tests for the detection of drugs in the
e. As most drugs are chiefly eliminated through the
neys, a knowledge of the processes to be employed for
r detection cannot fail to be of value from a diagnostic
nt of view.

The various sources from which the clinical facts em-
ied in this work have been gleaned are acknowledged in
General Bibliography, and in the Special Bibliography
ndividual drugs, which will be found appended. The
rences are arranged in the order in which they are
ted.

, West 40th Street;
*January 1st*, 1887.

# EDITOR'S PREFACE.

In the preparation of this reprint of Dr. Morrow's work for the New Sydenham Society I have endeavoured to go over the whole subject, as far as possible, with a view to check or supplement the author's conclusions. In this field I found but little to glean. I have also dealt with the literature accruing since 1887, and have to thank the author for kindly forwarding a number of references. Some additional ones, recent and older, which I have met with, are incorporated. The bibliography does not pretend to be exhaustive, but it is complete enough for all practical purposes, and comprises most of the important references or sources of information.

All the observations for which I alone am responsible are appended in the form of foot-notes. I trust that the little I have done may serve, in however small a degree, to increase the usefulness of Dr. Morrow's excellent book.

T. COLCOTT FOX.

London;
*July*, 1892.

# DRUG ERUPTIONS.

## HISTORY.

The literature of drug eruptions is essentially a new literature. While a few individual observations respecting the irritant effects of drugs upon the skin are found scattered here and there in the older medical literature, it is only comparatively recently that drug eruptions have been recognised as a distinct and clinically important class of affections. Most writers on Materia Medica and Therapeutics have passed over in silence the cutaneous manifestations of drug action, or have treated of them superficially and as of no practical importance. They were for a long time practically ignored by dermatologists, and it is only in the most recent text-books that they have been assigned a distinct place in the category of the dermatoses.

Lorry was the first dermatologist who called attention to the production of eruptions from the use of drugs. In his treatise, entitled 'Tractatus de Morbis Cutaneis' (1777) he says, "I have had many times occasion to observe in the course of my practice pruriginous, squamous, and miliary eruptions accidentally determined by the use of aromatic medicines, sudorifics, essential oils, &c."

Bell (1796) first described the irritant action of mercury upon the skin in the production of *eczema mercuriale*. Alley (1804) gave a more detailed description of the cutaneous eruptions caused by this drug, the accuracy of which a more extended observation has amply confirmed without adding much to its completeness.

Montègre (1814) described an eruption of urticaria from

the ingestion of copaiba. Since then many other forms of eruptive disorder due to this drug have been noted.

Rayer (1835) recorded numerous observations relating more particularly to the eruptive disorders caused by external irritants, which were classed by him as "artificial eruptions."

Ricord (1842) described various forms of eruptive accidents produced by iodide of potassium, the list of which has been largely increased by subseqnent observers.

Devergie (1857) called attention to the eruptive disturbances caused by arsenic. We are, however, chiefly indebted to the admirable thesis of Imbert-Gourbeyre for our knowledge of the irritant action of arsenic upon the skin.

Bazin (in his 'Leçons Théor. et Clin. sur les Affections Cutanées Artificielles,' 1862) made a systematic study of the cutaneous disorders provoked directly and indirectly by the action of drugs, and grouped them according to their elementary lesions.

Since then numerous observers, more particularly Bérenguier and Deschamps in France, Lewin and Behrend in Germany, Farquharson and Hutchinson in England, Piffard, Van Harlingen, and others in this country, have made a study of drug eruptions, and have added materially to our knowledge of their clinical characteristics, course, and pathogenesis.

## DEFINITION.

In examining the literature of "Drug Eruptions" there is found a difference in the signification of this term as employed by different writers. By many, changes in the skin caused by the external contact of drugs are excluded from this category, and the list embraces only those eruptive phenomena which follow the internal administration of medicines, and are connected with their absorption and elimination. Obviously, however, there is no well-grounded distinction between pathological effects determined by the same cause of action. In the case of many drugs, identical changes in the skin follow indifferently their external or

internal use, and these changes are not always limited to the portion of the integument with which the drug comes in immediate contact, but may be manifest on parts remote from the point of application. They are in many instances consecutive to the absorption of the drug, and are an expression of its constitutional action.[1]

By others the term has been limited in its application to the anomalous or incidental effects of drugs upon the cutaneous surface, in contradistinction to changes in the skin which are a more or less constant expression of the drug's physiological action, and which may be provoked for therapeutical purposes; evidently, however, a distinction based upon *motive in prescribing* is as fanciful as it is unscientific. The acneiform eruption of bromide of potassium, for example, occurs in a large proportion of all cases in which the drug is used, and its appearance is regarded by many authorities as the necessary evidence that the full therapeutic efficacy of the drug has been obtained. Although *designedly* produced, it is none the less a drug eruption. Individual peculiarity plays so important a rôle in modifying the action of drugs, that it is impossible to closely differentiate normal and specific from unexpected and anomalous effects.

In the proper signification of the term, Drug Eruptions *embrace all congestive and inflammatory changes in the skin caused by the external or internal use of drugs.*[2] This definition includes all eruptive disorders caused by external contact, as in industrial pursuits, intentional application to secure revulsive action, or for purposes of simulation, as well as those resulting from the introduction of drugs into

[1] There are a great number of vegetable, animal, and mineral bodies having an irritant action on the human skin, which, according to the author's definition of drug eruptions, might fairly be included in this work in addition to those given. I have not, however, enlarged the lines on which Dr. Morrow worked, nor have I thought it necessary to devote any space to an account of the dermatitis resulting from the external application of such medicaments as salol, naphthol, petroleum, paraffin, resorcin, pyrogallol, ichthyol, creolin, impure glycerine, lanolin, &c. The reader will find this work supplemented by Prof. J. C. White's book, 'Dermatitis Venenata.'—T. C. F.

[2] This signification would exclude *Argyria*.—T. C. F.

the system by absorption from the mucous membranes, the skin, or cellular tissue. The effect is the same, no matter through what channel of entrance the drug has gained access to the system.

## CLASSIFICATION.

A classification based upon the anatomical form of the lesions produced by drugs is impracticable. The very multiformity of the lesions forbids such an attempt for while the irritant action of a particular drug may in one individual be manifested by a single elementary lesion, the same drug may produce in another individual eruptive elements of dissimilar forms.

Bazin, applying the natural classification of Lorry to drug eruptions, divided them into two classes : *affections provoquées directes*, caused by the direct application of drugs upon the integument ; and *affections provoquées indirectes ou pathogénétiques*, including under this head every eruption produced by the introduction of a medicinal substance into the organism by way of absorption.

Under the title of "hematogenetic exanthemata," Behrend has classed drug eruptions as follows :—1st, eruptions occasioned by the specific action of drugs—acute in character ; 2nd, eruptions caused by the elimination through the skin of certain drugs—chronic in character ; 3rd, eruptions caused by the dynamic action of drugs which are, like the first class, acute in their development and course, but appear to possess a certain period of incubation.

In this work no classification will be attempted. The list of drugs will be taken up in alphabetical order, and the cutaneous phenomena exhibited by each will be examined in succession.

## GENERAL CHARACTERISTICS.

The symptomatology of particular drug eruptions will be considered under the head of each individual drug. Certain

haracteristics common to them as a class may be referred o in this connection.

While it is not possible to formulate with absolute pre-ision the distinctive characters of drug eruptions, or indicate lefinite features by which they may in every instance be recognised, and at once differentiated from the idiopathic affections of the skin, yet they possess certain special attributes which stamp them as a separate clinical class.

The polymorphism of drug eruptions constitutes a distinctive feature. Every possible lesion of the skin—macules, papules, wheals, tubercles, vesicles, bullæ, pustules, furuncles, ulcerations, gangrene, &c.—has been observed as the direct result of the use of drugs.

*The rapidity with which the eruption develops.*—Eruptions provoked by external irritants usually make their appearance within a few hours after the application of the exciting cause. The intensity of the resulting dermatitis depends upon the nature and strength of the irritant, the duration of its contact, and the sensitiveness of the skin. The difference in the susceptibility of the skin of different individuals to external irritants is markedly shown in relation to arnica, poison ivy, &c.

The length of time which intervenes between the ingestion of drugs and the first appearance of the eruption also varies according to the nature of the drug, the quantity administered, and the predisposition of the individual.

In general it may be said that certain forms, especially the erythematous and exudative, come out rapidly, from a few minutes to several hours after the ingestion of the drug, and vanish with the same celerity with which they appeared, if the offending agent be withdrawn. In other cases it may require repeated and long-continued use to develop the irritating effect upon the skin. In still another class of cases, small doses—smaller, indeed, than are required to produce the ordinary physiological effect of the drug—promptly determine violent tegumentary disturbance. It is noteworthy that, in exceptional cases, large doses of the same drug in the same individual may occasion no such effect. In these cases there would seem to be a reversal of the material law that increase of quantity carries with it

multiplication of power. In the case of eruptions which are common and typical, so to speak, which occur in a large proportion of all cases in which the drug is administered, as iodic or bromic acne, there is a measurable relation between the quantity of the drug ingested and the extent and severity of the lesions. In a majority of cases, however, the quantity of the drug ingested is immaterial, its irritative effects upon the skin being determined rather by the idiosyncrasy or susceptibility of the individual.

*Form.*—Drug eruptions differ in form and degree of severity, from the simple fugitive hyperæmia which rapidly fades, seeming to impress the skin so lightly that it leaves no trace, to the most violent inflammation, terminating in desquamation, sometimes exfoliation of the epidermis in large lamellæ or flakes.

The eruption caused by many drugs has a special form, not absolute and unvarying, but sufficiently so to be regarded as typical. This is especially the case as regards the irritant effects caused by the external application of drugs. The lesions caused by chrysophanic acid, tar, croton oil, tartar emetic, for example, are pathognomonic, so to speak. We recognise the character of the agent by its peculiar local action upon the tissues.

The eruptions determined by the internal use of many drugs is also characteristic; thus the eruption of belladonna is scarlatinoid; that of antipyrine, measly; that of the bromides, papulo-pustular. But it is well to remember that, coincident with this more common and characteristic form, there may be an accessory group of quite different eruptive elements, which may indeed substitute or take the place of the former. The multiplicity and variety of forms caused by the same drug depend not so much upon the quality of the generative agent as upon the mode of reaction of the individual, and upon other conditions imperfectly understood.

*Locality.*—The effect of irritants externally applied is usually limited to the parts exposed to direct contact, as the face, hands, and forearms, or to the vascular areas supplied by the affected nerves. Sometimes, however, the eruption overleaps these limits, and is manifested on parts

distant from the original focus of irritation.[1] Certain regions are more susceptible than others to irritant influence, such as the face and genitals, and, indeed, wherever the skin is thin and delicate, and rich in its nervous and vascular supply.

The eruptions caused by the internal use of drugs may be localised or generalised over the entire surface. There are certain regions affected from preference by individual drugs, upon which the eruption first appears, and from which it last recedes. The eruption is by no means limited to these predilected regions; they simply constitute points of departure from which the eruption becomes generalised if the use of the drug be persisted in. These peculiarities of localisation will be noticed when considering the action of individual drugs.

*The course* of the eruption varies; sometimes after attaining a certain development it persists in this form, and the indefinitely prolonged use of the drug provokes no additional phenomena. This is especially true of the acneiform eruption from bromide of potassium, which may remain practically unchanged for weeks or months. In the majority of cases, however, the eruption becomes, under the continued use of the drug, intensified in extent and severity, and new eruptive features may be added.

It is a noteworthy fact that the principle of *accoutumance*, by virtue of which the tissues become, from frequent exposure to any irritation, insensible to its action, does not come into play here. The textural predisposition of the skin to irritant action is not exhausted by habituation; on the contrary, it seems more quick to take offence at each new exhibition of the drug.

It has been observed that one attack of a drug eruption seems to confirm and intensify the susceptibility to subsequent attacks. While it may have required long and continued doses to determine the eruption in the first place, much smaller doses suffice to promptly redevelop a succeeding outbreak. There are rare cases on record in which this susceptibility has been overcome, or temporarily extinguished, by large and massive doses.

[1] See pp. 376, 377, and 380.—T. C. F.

In the case of persons who are exposed to external irritants, such as workers in quinine manufactories, in industrial occupations where arsenic and other poisonous dyes are used, it has been observed that the skin, though remonstrating by signs of irritation at first, acquires a certain immunity by habituation, so that the avocation can be pursued without serious inconvenience. It is to be noted, however, that this acquired immunity is readily lost if the person should cease his occupation for some time; upon resuming it the skin again protests, and immunity must be repurchased at the expense of more or less irritation for a variable time.

*The duration* of the eruption is usually sharply proportionate to the continuance of the exciting cause. While in some cases it may come out for some time after the use of the drug has been suspended, yet, ordinarily, improvement begins immediately upon the withdrawal of the offending cause. Its more or less rapid involution depends, of course, upon the character of the lesions and the recuperative powers of the individual. In certain diathetic conditions, when a latent predisposition to cutaneous disturbance has been awakened into activity by the drug, the eruption may persist indefinitely.

*The subjective sensations* which usually attend drug eruptions vary in intensity according to the nature of the inflammatory element. Sensations of burning, tingling, and the most intolerable itching are generally present, especially preceding the outbreak of the eruption and during its acute stage; in rare cases the eruption is completely indolent, and determines scarcely any subjective disturbance—the totality of the symptoms being expressed in the objective phenomena.

Drug eruptions are often accompanied by what are recognised as the ordinary physiological effects of the drug. Sometimes, however, the changes in the skin are attended with a set of additional symptoms which have nothing to do with the drug's normal action, such as fever and constitutional disturbance, more or less severe headache, and a general feeling of malaise.

If the use of the drug be persisted in after indications of intolerance have declared themselves, both the subjective

and objective symptoms become intensified, the whole system may sympathise, and a high grade of constitutional reaction be manifested. In some extreme cases, in which there is necrosis of the tissues and more or less profound ulceration, death may result from exhaustion.

## ETIOLOGY.

Etiology is commonly considered the weakest as well as the most difficult chapter of pathology. In the study of the causation of drug eruptions we have not to deal with mysterious agencies too subtle to be seen or demonstrated, and the nature of which can only be judged by their effects; the exciting cause of drug eruptions is material and tangible, and in the majority of cases this important element may be eliminated from the list of unknown quantities.

The nature of the exciting cause is ordinarily readily apprehended by the physician, or, in some cases, suggested by the patient, whose perceptions may have been enlightened by a previous similar experience, or who may be quick to grasp the relation of cause and effect between the ingestion of a drug and the disturbance which oftentimes swiftly follows. In most cases, if there be any doubt as to the causal connection between the drug and the eruption, it is resolved by a comparatively brief expectancy; for, as Bazin has remarked, in no other class of affections is the application of the old adage, *sublata causa, tollitur effectus*, so signally appropriate as here. Not only may the *quality* of the exciting cause be appreciated, but, unlike other causes of disease, its exact *quantity* may be definitely determined. It must be admitted, however, that in many drug eruptions the result is entirely independent of conditions of quantity, as it follows indifferently large or small doses.

If the efficient cause of drug eruptions be easily apprehended, the remote or predisposing causes still remain to perplex and baffle the physician; especially is the problem complicated by the existence of that etiological unknown—idiosyncrasy. Precisely as in the operation of other causes of disease, we find that susceptibility to the irritant

action of drugs varies in different individuals and under different conditions. The predisposing causes, such as climatic conditions, age, sex, heredity, &c., which exert such a modifying and controlling influence over the production of skin affections in general, play a rôle of minor importance here.

As regards the influence of climatic conditions, it has been observed that drug eruptions are more common in the summer season when the cutaneous functions are in the highest state of activity, and we may assume that all conditions which favour a fluxion to the surface predispose to the production of certain forms of drug eruptions.

The use of alcohol, teas, hot drinks, &c., which stimulate the cutaneous vascular system, are found to exert a marked influence in the production of the chloral rash, for example.

Age and sex seem in no way to dispose the skin to the irritant action of drugs, except from the accident of peculiarities of anatomical structure. As is well known, the texture of the skin of women and children is much less dense and tough than the same organ in man. This greater relative fineness and sensitiveness of the skin renders it more susceptible to take on morbid action, and thus more liable to eruptive disorders from any cause of irritation. It must be admitted, however, that the often-observed relation between a fine organisation of the skin and its susceptibility to irritant influences is by no means constant. We sometimes find that persons with thick and opaque skins manifest a peculiar aptitude to eruptive disorder, while persons with thin transparent skins are not at all liable to such disturbance.

Blond children with fine, delicate, succulent skins are especially liable to eruptive disturbances from the use of drugs; and, besides, the skin of all children is more irritable and prone to disorders of circulation from reflex disturbances.

Nervous irritability, hysteria, spinal irritation, and other neuroses which, from some unknown peculiarity of organisation, are much more common in women than in men, constitute what may be termed a neuropathic predisposition, which markedly modifies the action of drugs.

The comparative influence of heredity as a predisposing cause to drug eruptions is probable from the fact that idiosyncratic intolerance of drugs is rarely an acquired peculiarity. Observations bearing upon this point have not been collected in sufficient number to warrant deductions of a positive character.

Diathetic predispositions exert a marked influence in determining drug eruptions. This has been especially observed in the case of local irritants, the eruption becoming generalised and persisting long after the exciting cause has ceased to act. In these cases it is probable that the drug would be without pathogenetic influence, were it not for the predisposition to eruptive disorder constituted by the peculiar diathesis, the existence of which is a necessary condition of its operation. Eczematous subjects are particularly prone to drug eruptions. Numerous cases are recorded in which the slightest exposure to external irritants, such as arnica, carbolic acid, &c., has provoked into activity a latent eczema.

Scrofulous and lymphatic subjects are peculiarly prone to eruptions from the ingestion of drugs, which it has been observed are apt to be of a pustular character.

The most powerful predisposing cause of the determination of the irritant effects of drugs towards the cutaneous surface is the physiological predisposition known as *idiosyncrasy*. While the term is intrinsically meaningless, yet it is convenient to express that abnormal susceptibility to external impressions which is manifest in certain individuals —a condition which has been regarded as inexplicable as it is mysterious. The existence of idiosyncrasy as an etiological factor has been accepted as an ultimate fact, unknown and unknowable.

While we may not be able to draw aside the veil which shrouds this "mystery of individuality," yet it should not be allowed to obstruct what light may be thrown upon the explanation of its phenomena from our knowledge of the physiological properties of the tissues and their mode of reaction to external impressions.

Idiosyncrasy has been termed the bugbear of therapeutics; but this factor, as influencing the action of drugs, is

no more mysterious than the predisposition which is manifest in relation to the action of other exciting causes of disease, and which determines the morbid effect to this or that particular organ. To take a familiar example: of a certain number of individuals exposed to the action of cold, as in wetting the feet, the morbid impression may be reflected upon the respiratory mucous membrane, producing in one case sore throat; in another, bronchitis; in another, pneumonia or an attack of asthma: or it may be reflected upon different tissues altogether, producing in one case neuralgia; in another, rheumatism; in another, congestion of the kidneys, &c.; the same morbid influence determining disease of a particular organ, varied in form and intensity, or even different diseases. In the explanation of the mode of production of these phenomena we assume the existence of a textural predisposition in the affected tissues, constituted, it may be, by inherent weakness or antecedent disorder, which renders them *partes minoris resistentiæ*.

So, also, the determination of the irritant action of a drug towards the cutaneous tissue implies either the existence of structural peculiarities of the skin, enfeebling its capacity of resistance, or a heightened susceptibility of the nerves which regulate the circulatory and nutritive processes of this organ. It is by no means clear whether this morbid aptitude of the skin to irritant action is due to anatomical or histological alterations in the cutaneous tissues, too subtle to be seen or demonstrated, or to an abnormality of the nerve-element, which may be expressed as "erethism" or "irritability."

Begin defines idiosyncrasy as "the predominance of an organ, a viscus, or a system of organs." Experimental investigation has demonstrated that "the law which governs the susceptibility to the action of drugs is, that the more highly specialised any system is, the more readily it is affected by a medicinal agent." We find in persons most susceptible to anomalous eruptions that the nervous element or temperament predominates. Neuropathic, hysterical individuals, those who suffer from any of the protean forms of neurasthenia, are precisely the persons most liable to manifest idiosyncratic intolerance of drugs.

Conjoined with this highly wrought nervous organisation, he skin itself may be more highly differentiated by fineness nd delicacy of structure, and endowed with a more exqui- ite sensibility.

We may conclude, then, that a predisposition to drug erup- ions may inhere in the skin from some congenital structural peculiarity constituting a "native debility" of this organ, or it may reside in a peculiarity of the nervous organisation, characterised by an abnormal sensitiveness of the vaso-motor system to irritant influences.

## PATHOGENESIS.

There is a difference of opinion among writers as to whether these eruptions should be classed among the phy- siological or toxicological effects of the drugs producing them. The term pathogenesis, implying a pathological pro- cess, is employed with a clear recognition of the close lines which unite the physiological and the pathological. As pathological states are but modifications of the healthy state, so the toxic effects of a drug differ in degree, but not in essential nature from its physiological effects: there is no definite limit where the one ends and where the other begins. A certain proportion of drug eruptions are an expression of the drug's physiological action, while others are altogether incidental, depending upon conditions of the organism which in the present condition of our knowledge are obscure and imperfectly understood.

### ERUPTIONS FROM THE EXTERNAL USE OF DRUGS.

Excluding from consideration the class of agents known as escharotics, we will first briefly refer to the changes in the skin caused by the external application of certain drugs. The links in the relation between cause and effect are here distinctly traceable, and the mechanism of their action is explicable on purely physical and chemical grounds. The intensity and severity of the congestive and inflammatory disturbance produced depend upon the nature of the agent employed, the duration of its contact, and other circum-

stances, such as the sensibility of the skin and the mode of reaction of the individual. Certain effects, to be considered later, are the result of the absorption of the drug through the skin, and analogous to those which follow its internal administration.

A clinical distinction may be made between effects which *invariably* follow contact with certain drugs, and those which are *occasional and irregular* in their manifestation.

The *first class* of effects is determined rather by the nature of the drug than by any peculiarity of organisation or mode of reaction of the skin. They are so constant and characteristic that we may recognise the nature of the agent employed by the form of its lesion. The blebs of cantharides, the pustules of antimony and croton oil are characterised each by a special evolution, and are as typical in their forms as are the pustules of variola. We cannot explain why the irritating influence of different drugs is exerted upon different constituent elements of the skin, any more than we can explain why the pathological changes met with in measles should be grouped around the blood-vessels and glands, while in scarlatina the pathological process affects the tissues proper of the derma as well as the cells of the epidermis.

In general, it may be said that the effect of a cutaneous irritant is limited to the vascular area supplied by the affected nerves. The irritating effect may sometimes pass beyond this limit and invade adjacent portions of the skin, or it may be diffused over the entire surface. This may be explained by what has been termed the "contagion of continuity," or upon the assumption that it is due to the absorption of the drug, and is an expression of its constitutional action.

The *second class* of effects is far from being constant. Their production seems to depend less upon the intimate nature of the exciting cause than upon a specific predisposition of the cutaneous tissues to disordered action, which may be expressed by the term *morbid aptitude*.

As in the case of anomalous eruptions from the internal use of medicines, the eruptive form is determined rather by the individual than by the drug. Thus we recognise in

"tar acne" the specific irritating effect of tar upon the cutaneous tissue; but in one individual the use of tar may produce a simple dermatitis; in another, erysipelas;[1] in another, a pustular or a furuncular inflammation; while in the large majority of individuals it will cause no eruptive disturbance whatever, the difference of the effect depending upon the reaction of the skin in the different individuals.

This variation in susceptibility to irritant influences of the skin of different persons may depend upon physiological conditions, such as a greater fineness or delicacy of texture, or upon a peculiar excitability or irritability of the sensory nerves, which disposes them to take offence at the slightest provocation. We find that this vulnerability of the skin which renders it abnormally incapable of resisting disturbing influences is manifest in relation to poison ivy, vegetable parasites, the exciting causes of eczema, and, in fact, all external irritants.

The cutaneous changes caused by the external application of drugs admit of a simple explanation. The drug acts, just as caloric or mechanical irritants do, upon the nerve-element alone, the resulting changes being phenomena of irritation. The irritation of the peripheral extremities of the sensory nerves causes a paralysis of the vaso-motors of the vascular area affected, which results in dilatation of the blood-vessels, and which may go on to typical inflammation of the skin with exudation.

In the first class of cases the specific character of the irritant determines the eruptive form; in the second class the response to the stimulus is materially modified by the physiological properties of the tissues affected.

### ERUPTIONS FROM THE INTERNAL USE OF DRUGS.

We come now to a consideration of the cutaneous disorders which result from the introduction of drugs into the system by way of absorption. Instead of a direct irritant influence upon the skin, the drug stimulates all the blood-containing organs with which it comes in contact. It affects the centres of sensibility as well as the peripheral nerves,

[1] Erysipelas-like inflammation.—T. C. F.

and the pathogenetic mode is much more mysterious and difficult of comprehension.[1]

The eruptive disturbances which follow the internal use of drugs may be divided into two classes.

1st. *Common, specific eruptions,* which are more or less characteristic in their anatomical form, mode of development, and locality affected, and which are associated with the other physiological effects of the drugs.

2nd. *Incidental, anomalous eruptions,* without distinctive form or character, which manifest dissimilar eruptive elements, and which may be associated with the physiological effects of the drug, or merely incidental thereto.

*Eruptions of the first class,* of which "bromic acne" may be taken as the type, must be regarded as an expression of the specific action of the drug upon the cutaneous tissues, as much so as its other physiological effects upon the general system. They occur in a large proportion of all cases in which the drug is administered, and they are evidently determined by the inherent properties of the drug.

*Eruptions of the second class* must be considered as an aberration of the drug's normal action, the deviation from the typical mode of action being determined by the forces of the organism through which it operates. They may be caused by drugs which neither commonly nor specifically act upon the skin, the necessary condition of their development being a predisposition or aptitude inherent in the individual.

In this connection it may be well to recall some of the more characteristic features of drug eruptions. In the first place, it must be borne in mind that the same eruptive form

[1] When a drug is ingested it is conceivable that in consequence of a toxic action, *e.g.* on the stomach, an influence is reflected through the vaso-motor system to the skin, and so an eruption, *e.g.* urticaria, is excited. So also with regard to medicaments introduced into the rectum or uro-genital system, and perhaps hypodermically. When the drug or its product circulates in the system it might exercise an influence (1) upon the vaso-motor or trophic centres (central or peripheral); or (2) upon some particular tissue or organ, such as the peripheral nerves or the skin itself; or (3) it might prove irritating during its elimination by the skin glands; or (4) occasion an eruption by the sudden excessive excitation of a function, such as sweating; or (5) act on the blood-mass or vessels.—T. C. F.

nay be produced by different drugs, and that the same drug nay produce a variety of eruptive forms. It is not possible, herefore, to establish a distinction between these classes based exclusively upon the anatomical form of the lesions, since one drug may exhibit characteristics of both classes. Thus the type of the quinine exanthem is erythematous, but exceptionally it may be eczematous or purpuric. Iodide of potassium ordinarily produces a papular or pustular eruption ; but instead, or indeed coincident with this specific form, there may be an anomalous eruption of dissimilar forms. In cases reported by Pellizari and myself, for example, side by side with the common acneiform eruption there were bullæ, tubercles, ecthymatous pustules, and large subcutaneous nodules, which evidently must be classed among the rarer incidental effects of the drug.

Again, a drug eruption, the type of which is erythematous, may, under special conditions, such as the prolonged continuance of the exciting cause, be developed into a papular, vesicular, or pustular eruption.

In other cases there is no mutation of forms ; the indefinitely prolonged use of the drug will be unattended with any essential change in the character of the eruptive element. If it commence as a papular or a pustular eruption, it will continue as such, independent of the dose or duration of the drug. It is to be noted, however, that when the lesions are in process of involution, if the drug be renewed, it will cause a *poussée subintrante,* and we may have different forms side by side, some in active evolution, others representing the acme or completion of the morbid process, while others are on the point of disappearance.

We perceive, then, that in endeavouring to appreciate the mode of production of these eruptions it is impossible to adhere closely to the distinction between specific and anomalous eruptions, since there is nothing absolutely constant or characteristic in their respective forms ; they are as varied in their manifestations as are the physiological peculiarities of the individuals producing them. It is to be observed, however, that difference in effect does not necessarily imply difference of mode of impression. We think that most writers err in attempting to differentiate pathogenetic modes

upon the basis of difference in anatomical form of the lesions. Anatomical form is as misleading in pathogeny as it has proven defective as a basis of classification.

Notwithstanding the diverse character of drug eruptions as indicated above, we have seen that they all possess one distinctive generic feature, which stamps them with the seal of a common causality of origin—they always promptly disappear on the withdrawal of the exciting cause. The more or less rapid removal of the cause is of course subordinate to conditions of elimination, the celerity of this process varying in the case of different drugs. The rapidity of the disappearance will also vary according to the nature of the lesions; obviously the slight cutaneous disturbance expressed by a simple erythema would not require the same time for its involution as the more profound tissue changes represented by an inflammatory nodule or an ecthymatous ulcer. Again, it is to be borne in mind that diathetic predispositions awakened into activity by an irritant drug may impress the character of chronicity upon the resulting skin lesions—the inflammatory fluxion to the surface persisting long after the cause which determined it has ceased to act.

Leaving out of consideration for the present that mysterious factor expressed by the term idiosyncrasy, let us examine the various theories which have been put forward as to the mechanism of the production of these eruptions.

In the first place, it may be said that an explanation of these incidental cutaneous phenomena has been sought for in the *quality of the drug*. It was naturally inferred that the production of unusual drug effects must be caused by an impurity of the agent used, due to its faulty mode of preparation or its accidental admixture with toxic principles, &c. With this view, other preparations of the same drug have been substituted, the alkaloid for the crude drug, and *vice versâ*, with the result of the production of identical irritant effects upon the skin. So that the assumption of a possible impurity of the drug as the efficient cause of these irritant effects upon the skin must be dismissed as groundless and disproved by careful experimentation.

The theory which has been adopted by most writers on

this subject is, that a large proportion of these eruptions are caused by the elimination of the drug through the skin.[1]

The theory of the elimination of drugs through the cutaneous glands is based upon the assumption of the existence of one of two conditions as determining causes. 1. *Impairment of the integrity of the eliminating organs.* 2. *Elective affinity of the drug for the constituent elements of the glands.*

The hypothesis of the impairment of the integrity of the eliminating organs as a determining cause is based upon the view that since almost all drugs introduced into the system are normally eliminated by the kidneys, when from any cause this channel of egress is blocked up, the skin by virtue of its vicarious functions attempts to perform the work of the kidneys, and the drug in its passage through the cutaneous glands causes irritation, which is manifested by various lesions. This theory, which has been urged with some plausibility by Farquharson, seemed to gain support from clinical facts. Several cases were cited in which the use of the bromides and iodides caused severe cutaneous disturbance, and the patients were found suffering from renal inadequacy and cardiac lesions. But further clinical inquiry has not demonstrated anything like a constant relation of cause and effect between severe renal disease and a special liability to a determination of drug action towards the cutaneous surface, even where the pathological alterations were of such a nature as to incapacitate these organs for the proper performance of their functions.

This theory pushed to its legitimate conclusion would attribute all drug eruptions to cumulative action, on the principle that introduction should in all cases be compensated for by elimination—the maintenance of this equilibrium being the condition of normal drug action. In other words, that "saturation of the system" with a drug must occur as a preliminary or necessary condition of the production of its incidental effects.

This assumption is, however, abundantly disproved by clinical facts. We find that the smallest dose of a drug will, in many individuals, promptly produce the most violent tegumentary disturbance; while in others, massive doses of

[1] The result of a direct local irritation (Bazin).—T. C. F.

the same drug may be continued during long periods with absolutely no effect upon the cutaneous surface, the result being entirely independent of the *quantity* of the foreign element circulating in the blood. In the analogous cases of eruptive disturbance *ab ingestis* we recognise that it is the *quality*, not the *quantity*, of the irritant that offends.

Another phase of the "saturation of the system" theory is that the foreign material accumulates until Nature, unable longer to tolerate its presence, concentrates her forces and makes a grand parturient effort to expel the offending material through the cutaneous pores, and in this process the skin suffers various lesions of continuity. This theory is akin to the now obsolete one which recognised in the roseola of syphilis, and the exanthem of the specific fevers, an evidence that the poison had been driven to the surface and was in process of expulsion.

The second hypothesis is that drugs have an affinity for special anatomical elements, and that, by virtue of this selective action, certain drugs are attracted towards the cutaneous glands.[1] Physical and chemical evidence of this pathogenetic mode is furnished, it is claimed, in the anatomical seat of certain lesions, as the sebaceous glands in iodic and bromic acne, and in the demonstrated presence of the drug at fault in the lesions which it has caused. No absolute proof that either of these conditions is a constant occurrence has been adduced. While the follicular apparatus may be incidentally involved in any morbid process affecting the skin, there is no evidence that it is the exclusive seat of these lesions.

On the contrary, careful and minute investigations into the anatomical seat of iodic and bromic lesions have shown conclusively that, in many cases at least, the sebaceous glands were unaffected. Drs. Thin and Duckworth concluded from their investigations of iodine lesions that they were not of the nature of acne; microscopical examinations showed no implication of the sebaceous glands and hair-follicles. Negative evidence is also found in the fact that these lesions occur in

[1] Another theory is that the skin responds to the irritation set up by the drug as it circulates in the blood, not necessarily during glandular elimination, just as peripheral nerves may be picked out by various toxic agents.—T. C. F.

cicatricial tissue, and in regions where sebaceous glands do not exist. Other observers have furnished positive proof that these lesions are of the nature of a localised dermatitis, in which the glandular structures may be healthy, or only incidentally involved.

Proof of the second proposition is also sought for in the fact that the drug has been found in the contents of certain lesions—detected in the act, so to speak. But absolute proof of the production of these lesions in this way cannot be adduced. So far from being a constant phenomenon, we are justified in regarding it as a mere accident or coincidence, since numerous observers have failed, even with the most carefully conducted tests, to detect the presence of the drug in the cutaneous lesions, while it was freely found in the urine. If the elimination of the drug through the glands be the cause of the disturbance, its presence should be a constant feature. Again, if the matter were reduced to a simple chemical combination between a certain drug and the glandular elements, then this action should take place every time and in every case where these two factors were brought into contact. On the contrary, instances are exceedingly rare in which such a reaction could by any possibility be alleged.

Trousseau sought to establish an identical pathogeny for sudoral and drug exanthemata, claiming that both were caused by a modification in the composition of the sweat, which took on an irritant quality, and in its passage through the cutaneous emunctories betrayed this irritation by a variety of pathological lesions. But proof that these lesions are not caused by an irritant and exaggerrated sudoral secretion is found in the fact that two drugs, opium and belladonna, both produce a scarlatiniform eruptiom. The specific action of one is to stimulate the functional activity of the sweat-glands, while that of the other is to diminish or suppress this function altogether. Further proof that eruptive disturbances are independent of the functional activity of these glands is furnished by the fact that the existence of the condition known as unilateral sweating does not modify the symmetrical development of a drug exanthem. In a number of such cases reported there was no difference in the rash on both sides.

Admitting that the eruptive disturbances which follow the ingestion of certain drugs are the result of modifications in the glandular tissues, associated with increased functional activity, we see in this only an evidence of the direct influence of the drug upon the special nerves which regulate the secretory functions of these glands. Recent physiological research has demonstrated the existence of special secretory fibres, which are distributed to the salivary and sweat glands, and which regulate their functional activity independent of conditions of hyperæmia. It has been conclusively shown by Sartisson that the absorption and elimination of iodine by the salivary glands, for example, is due, "not to chemical affinity of the drug for the substances of which the gland is composed, but to nerve influence alone;" so that either functional or structural changes in the sweat-glands point to a disordered innervation, the determining cause of which must be sought for in the action of the drug upon the special nerves which supply these glands.

The "elective affinity theory" must therefore be dismissed as improbable. There is no evidence that the cutaneous glands or other tissues of the body exert any influence upon drugs which is at all of the nature of attraction.

Behrend classes drug eruptions under the title of "Hæmatogenetic Exanthemata," on the theory that they are for the most part due to changes in the blood susceptible of clinical demonstration. He assigns special prominence to what may be termed the dynamic theory. He asserts that all drug eruptions, with the exception of the erythemas caused by the specific action of belladonna, hyoscyamus, stramonium, and perhaps arsenic, and the acneiform and pustular eruptions commonly seen after the use of the bromides and iodides, more rarely after arsenic, are caused by the dynamic action of drugs. This effect, he claims, is entirely independent of the physiological and therapeutical action of the drug, but due to the agency of a foreign material probably of chemical nature, generated in the blood by reason of the presence of the drug in the system.[1]

[1] As Behrend's views are but ill-understood in many quarters, I may add a few words in further explanation. Medicinal eruptions, he says, are in point of view of form and evolution quite independent of the chemical or

Whether this foreign material is produced by catalytic action, or is the result of a direct combination of the drug with a hypothetical substance in the blood, is not specified. It is singular that this mysterious chemical compound should be so potent for mischief and yet so indefinite in substance that its detection transcends our powers of analysis. This hypothesis seems as fanciful as it is utterly untenable. It is merely a modification of the old humoralistic view which attributed all pathological alterations to a dyscrasic condition of the blood. Besides, this theory is irreconcilable with clinical facts. If the changes in the skin be caused by a changed blood-mass, they should not be confined to restricted localities, as is often the case, but should be manifest everywhere the blood circulates.[1]

pharmaceutical nature as well as the physiological and therapeutic effects of the substances producing them. Etiologically two groups can be formed. Firstly, the iodic and bromic *pustular* eruptions, characterised by the fact that (1) they only appear after prolonged usage of the drug, when the organism is thoroughly impregnated; (2) that they occur more or less in all persons submitted to its influence, whilst variations with regard to precocity and delay, &c., are due to relative susceptibility; (3) that thick skins actively secreting sebum are probably more liable to attack, and certain vascular regions; and (4) that the eruptions of this group are probably due to local irritation from the excretion of the drug by the cutaneous glands. Secondly, the more acute and more extended exanthematic rashes. He thinks that the contrast between the minuteness of the dose in many cases and the great extent of eruption negatives any direct action of the drug. Arrived in the blood these substances undergo chemical transformations, the products of which lead in certain individuals, predisposed by certain qualities of their tissues, to the cutaneous trouble in question. He formulates two laws for them, viz. (1) that in external conditions apparently absolutely similar the same medicament can provoke in different persons exanthems completely different; (2) that in the same individual the same medicament gives rise always to the same eruption.

Trousseau, in his 'Traité de Thérapeutique,' refers to this mysterious dynamic property of certain substances. He held that these eruptions are not developed like artificial lesions and diseases directly by poisons in healthy persons, but are morbid properties latent in our organism, which every poison excites by impressing on these properties special characters according to their special nature. The poison, therefore, is not the disease, but its determining cause.—T. C. F.

[1] As an introduction to the discussion on drug eruptions at the International Medical Congress held at Berlin in 1890 Dr. Brooke presented the

following conclusions, arrived at by Prof. von Dühring and himself. The question to which their consideration was more specially limited was the following:—"Are the dynamic eruptions of Behrend to be separated completely from those which he calls specific?"

"The most striking feature which presents itself on reading through a large number of accounts of individual drug eruptions is the fact that so many substances of totally dissimilar chemical constitution are capable of producing one and the same exanthem; whilst, on the other hand, the same substance produces in different individuals very different eruptions.

"For the explanation of these seemingly very contradictory phenomena there must exist some means by which the actions of these apparently illimitable causes are practically reduced in number by being conducted into a limited number of channels, whilst at the same time these means must offer some explanation of the fact that each of these channels may be entered by any one of the various causes.

"In this process of limitation we must keep in mind that idiosyncrasy plays the chief rôle. The only constant factor is the relation of one drug to one individual, and from this it follows that the particular mode of limitation in each case must be dependent on the peculiar bodily constitution of the individual.

"So far as I have been able to see, there has been yet only one attempt made to offer any explanation of this process, and this was the one which was made by Behrend. He brought forward the very attractive hypothesis that the drugs did not produce their cutaneous phenomena by their direct action, but through the agency of a limited number of chemical substances (now called 'toxines') which are engendered in the body under their influence. It is seen at once, by this hypothesis, that a process of reduction in the number of the causes of the drug eruptions actually takes place; and further, that it is quite possible for the same drug to give rise to different toxines in different individuals. Thus, according to Behrend's view, the question resolves itself into one of pathological chemistry, and by isolating and studying these chemical products we ought to be able to discover the key to the comprehension of the *modus operandi* of the drugs in causing the eruptions. But before entering into this laborious investigation it would be advisable to inquire as to whether the hitherto known facts really and of necessity lead us to this same hypothesis, or if this limiting process can be possibly explained in any other way.

"In the case of those drug exanthemata with which we are here concerned we have to do chiefly with angioneuroses, and we set on one side all such eruptions as are either of a purely inflammatory nature or present the characters of new growths as being too distantly removed from the schema of the majority to allow of their simultaneous consideration. The greater part have a nervous character, and we shall do well in our present inquiry to proceed by investigating the nervous condition of an organ which, on account of the anatomical arrangement of its nerves, lends itself more easily to the study of the nervous phenomena than does the skin. We have long been, for example, in possession of accurate knowledge of the exact influence of various drugs upon the different functions of the nerves which

supply the heart, and if we cast a broad glance over these reactions we are quickly able to divide them into three classes, according to the actual effect which the drugs possess. We know of some drugs which have so strong an influence on the hearts of the enormous majority of people that we are able almost with certainty to predict their exact effect, *e. g.* digitalis. These drugs seem to have a powerful selective action on certain special points of the cardiac nervous system. Since the reaction is concentrated in these cases upon one or the other centre, or particular portion of the nerve course, the effect seems to present a certain regularity in all subjects. It would be possible to speak here of specific action in the same sense in which Behrend has applied the word in regard to certain drug eruptions.

"There are other poisons which act upon the heart, the effects of which are not so regular in their manifestations as to be always quite the same in all persons. In these it seems that the selective action is not so decided on particular portions of the nerves as to create always the same effect. In consequence of this diminished selective power, only a smaller number of people react at all, and these not so regularly. Thus, for example, there are some the action of whose heart is comparatively immune to nicotine, whilst in others it produces great irregularity and depression.

"And there are, again, a third class, in which the selective power is so slight that in most persons there is absolutely no observable effect. In certain persons we may observe some effect, but the effect is quite irregular, and cannot be predicted. In these we must presume that the relation of the drug to the heart nerves is an exceedingly slight one, and that only very seldom does the one or other influence come more to the front.

"From this brief reference it will be seen that we have to deal with a regularly descending series, which passes from those types of drugs which are perfectly regularly in their action, through those in which the influence is much less certain, down to those in which, if exerted at all, it is of an exceedingly irregular character. In this last class we reach what we may with justification call a true idiosyncrasy.

"I believe that it speaks for itself that the influences which act upon the nerve system of the skin follow the same rules. Here, too, we have to distinguish between a whole series of different ganglia and nerve endings. We must assume that there are drugs which are able to affect separate centres or nerve leadings in an isolated manner. Where this happens we must find the same phenomena regularly produced in the same individual. I will instance, for example, amyl nitrite, the action of which produces a flushing of the face, so that we can see that certain centres controlling the supply of blood to the face have a well-defined connection with this drug. This we may well call a specific influence, and it is to well-pronounced and constant phenomena of this class that I would wish to reserve the title of specific action. Without doubt we have other drugs the effects of which are directed on to the nerves of the skin, but in a less precise manner, so that they are neither so general nor so regular in their external effects. In this class we may instance belladonna, hyoscyamus, and stramonium.

"But by far the largest class with which we have to deal is that of those drugs, the outward manifestations of which, so far from exhibiting any

constancy, tend to produce a very large and variable series of angioneurotic phenomena, which differ in every individual. Of this class, which makes up the bulk of the angioneurotic group, we have numerous examples, from which we may cite quinine, chloral, and antipyrin.

"The greater or lesser universality or specificity of the angioneurotic eruptions which we have so far considered, their topography, their greater or lesser intensity and duration, all these seem to be explicable by means of the physiological difference of function of the nerve-centres and nerve-terminations in the skin. The eruptions produced are common or rare, universal or circumscribed, general or predilecting certain regions, intense or weak, according as to whether the sensitiveness of that particular portion of the nervous system which is involved in their production is easily affected by particular drugs in the majority of people, or whether it is a peculiarity only found in a few.

"I see no clearly defined differences between the specific and dynamic rashes of Behrend, but rather a continuous and gradually progressive series, extending from those which occur with almost absolute regularity to those which vary in every individual. From this point of view it becomes easily intelligible why most of the exanthems are of such an irregular and unpredictable nature. But, on the other hand, I am not prepared to believe that the limitations in the *modus operandi* of the drugs, which must take place in order to account for the fact that so many different drugs manifest their action under the guise of similar types of eruption, are completely explained by any special influence exerted on certain parts of the nerve-system of the skin. Here we must absolutely recognise and concede an influence which springs from the peculiarities of the individual skin itself. How this individuality may account for the real drug exanthems we must now consider.

"If we picture to ourselves a schema of the skin from which we have abstracted the tissues of the skin proper, thus leaving only its vascular system and the nerves which supply it, and ask ourselves what could be then the influence of all the drugs which we know to be capable of producing exanthemata, we find their general influence must be confined to the production of hyperæmia. All the many-sided phenomena of the drug exanthemata are therefore, as far as the vascular system is concerned, reduced down to one single element, the vascular paralysis or hyperæmia.

"This reduction down to one element is, however, far greater than we have any necessity for in order to explain the limitations of the exanthemata. The vascular system of the skin, so far from being surrounded by indifferent structures, is embedded in a richly organised mass of tissues of extraordinary individual variety. This very fact gives us the explanation of the strikingly different lesions which occur among the angioneurotic exanthemata. When a simple paralysis occurs we have a simple erythema, which can, when the epidermis has little power of resistance, give rise to vesiculating and bullous erythemata; or again, when a spastic element concurs, the erythematous basis may develop into papules like those of erythema multiforme and nodosum, or into wheals; or finally, where a passive condition (Stauung) takes the place of the active hyperæmia, con-

We come now to a consideration of the theory of the neurotic origin of drug eruptions—a theory which recognises the intimate dependence of all cutaneous changes, whether slight and transient, or more profound and persistent, upon disorders of innervation.

While, at first glance, it may appear inconsistent to group together eruptions so multifarious in form and character, and attribute the same pathogenetic mode to drugs

ditions of purpura and œdema may be produced. All these different types depend not on the constitution of the vascular and nervous system, but on the peculiarities of the skin itself, and vary according to its individuality.

"Thus we see that the limitation of these seven main types and their connecting links are, after all, not so very remarkable a one as is generally believed. On the contrary, we have seen that they all arise out of the one common element of hyperæmia as worked upon by the complex peculiarities of the tissues of various skins.

"Behrend, setting out from the assumption of the specific action of a few drugs, has come to the belief that with most of the others, where he could not find a specific exanthem, there must probably be a distinct substance formed in the body by the action of the drug which could account for the peculiar appearance presented by the exanthem. This supposition will be seen, I think, from the explanation which has just been given, to be an unnecessary one. The statement that the various drugs, when hypodermically injected, do not give rise to exanthemata, if correct, would tend to support Behrend's view, but the instant production of general urticaria by the very superficial injection of certain substances, as by the nettle or the flea, or by the simple crushing of a strawberry or raspberry in the mouth, cannot be readily explained on the supposition of the action of intermediate agents.

"Thus, as I regard the question, we can, as we follow the drugs first in their influence on the nervous system and then on the skin itself, explain the different peculiarities which distinguish the purely angioneurotic drug exanthemata.

"But, in dependence on these, we come easily to an explanation of that smaller group of drug eruptions in which the angioneurotic symptoms are combined with more pronounced signs of inflammation, as when we see after quinine not only an erythematous rash, but even a long-standing scarlatiniform hyperæmia with immense shaling of the cuticle. Here we have to recognise, in addition to the angioneurotic influence of the nerve-centres, a local direct influence of the drug circulating in the blood on the tissues of the skin themselves.

"As regards the purely inflammatory and also the fungating processes which may follow the ingestion of drugs, it is understood that they do not fall within the range of the angioneurotic lesions of which I have spoken, and to which my investigation has been confined."—T. C. F.

widely varying in their physiological action, yet there are many considerations which force us to the conviction that it is in the sphere of the nervous system that we must look for an explanation of these phenomena. In the light of our present knowledge respecting the primary action of most drugs upon the nervous system, such a pathogenesis of these eruptions is not only conceivable, but reasoning from analogies with other cutaneous phenomena, the neurotic origin of which has been demonstrated, it appears extremely probable.

The analogies existing between changes in the skin provoked by the direct contact of drugs and those resulting from their internal administration should not be ignored. Both classes of effects are due to the same cause of action; the inflammatory process is identical, and they exhibit the same eruptive elements. So far as the anatomical form of the lesions is concerned, there is no difficulty in attributing to them the same pathogenetic mode. We have seen that almost every possible lesion of the skin—erythema, papules, pustules, vesicles, bullæ, wheals, furuncles, gangrene, &c.—may be determined by the application of external irritants. The mechanism of this production is simple and evident. There is no elimination of the drug through the cutaneous glands, no possibility of a changed blood-mass, no generation of a "chemical compound" from the presence of the drug in the circulation.

The inflammatory changes in the skin are caused through the agency of the nerve-elements alone. The irritant applied to the surface of the skin affects its sensory nerves, and the inflammatory phenomena appear in the vascular area which they control. Is it not fair to assume that precisely similar phenomena may result from a direct impression of an irritant agent circulating in the blood upon the vasomotor centres or upon the peripheral distribution of these nerves?

In studying the symptomatology of drug eruptions, we find that a large proportion present the characters of simple cutaneous congestions, associated with sensory disturbances more or less severe. Usually the nervous symptoms precede the development of the exanthem.

These congestions appear suddenly, and may affect only certain cutaneous regions, or they may become generalised, according as the disordered innervation is limited to particular vascular areas or affects the entire cutaneous vascular system. The character of the changes impressed upon the skin will depend upon the blood-stasis, whether it be transient, or prolonged and intense.

In some cases, no doubt, these congestions are purely reflex phenomena, the point of departure of which is irritation of the sensory nerves of the gastro-intestinal mucous membrane. They are analogous to urticaria *ab ingestis*, and reflex changes in the skin from irritation of a peripheral nerve, as in traumatism. Besnier attaches considerable importance to this pathogenetic mode, and proposes to circumvent it by introducing the drug hypodermically. Unfortunately for this theory, it has been proven that the dermatopathic effect is, in the case of most drugs at least, entirely independent of the mode of their introduction into the economy. It is probable that irritation of the terminal filaments of the pneumogastric accounts for but a small proportion of these cutaneous disturbances.

The large majority are consecutive to absorption of the drug, and due to its specific action upon the peripheral nerves or nerve-centres. Whether this influence be exerted primarily upon the vaso-dilator or the vaso-constrictor nerves, the ultimate effect is vascular dilatation, and if the congestion be sufficiently intense, exudation. We recognise the erythematous and urticarial eruptions of antipyrin, arsenic, belladonna, bromide of potassium, chloral, copaiba, digitalis, hyoscyamus, opium, morphia, quinine, stramonium, salicylic acid, &c., as angioneurotic phenomena, caused by the specific action of the drugs in question upon the vaso-motor system.[1]

[1] For the discussion on drug eruptions at the International Medical Congress held at Berlin, 1890, Colcott Fox sought an answer to the question, "Are the wide-spread erythematous and vesicular eruptions arising after the circumscribed (local) external application of certain drugs, such as iodoform, sublimate, belladonna, chrysarobin, arnica, &c., to be placed in the same category with the universal eruptions following the internal use of the drugs?" He classified the effects produced in three groups, viz.:

I. Effects strictly local, and limited to those regions with which the drug

The similarity in these eruptions to other cutaneous phenomena, the nervous origin of which is recognised, would argue similarity of pathogenetic mode. It is now accepted that the roseola of syphilis, the prodromal rash of variola, the exanthem of measles, scarlatina, typhoid fever, &c., are due to the direct action of an irritant, the specific virus of the particular disease, upon the centres which preside over vaso-motor innervation. We may reasonably infer a like

comes in contact; due directly to superficial local irritation, and occurring without any systemic reaction.

II. Effects also local, and due to peripheral action, but not coterminous with the site of application of the drug, and radiating for some distance around; occurring with or without systemic reaction.

(α) In which the eruptions are limited to the seat of application of the drug and a zone or areola around.

(β) In which the eruptions spread continuously from the site of application over a more or less wide area, to use Dr. Unna's striking phrase, like water in blotting-paper.

III. Radiating effects due to more central irritation, with or without coincident systemic reaction.

(α) Eruptions which begin locally from peripheral irritation and spread, and are followed by the evolution of remotely situated areas due to a central irritation.

(β) More or less widely spread or generalised eruptions, beginning either near the site of application of the drug or remotely in several places, without local signs, and due to a purely central irritation.

In the first group are comprised those eruptive lesions which appear to be simple local irritative effects. Even here the vulnerability varies widely. If the irritant be volatile, like the rhus poisons, or arseniuretted hydrogen, or of a very light powdery, scaly, or crystalline character, such as chrysarobin or iodoform, and if in addition it be applied in profusion or under circumstances which permit of dissemination, *e. g.* the loosening of dressings, the contact of contiguous surfaces of skin, scratching, rubbing, &c., then the eruption may extend over a remarkably wide area in quite a surprising manner.

A study of the second group demonstrates—

1. That the method of application, and the amount of drug used, entirely precluded in many cases all possibility of the irritating agent being widely diffused over the surface.

2. That in some cases the irritant effects are not manifested till the drug is absorbed; or, at any rate, do not at once declare themselves.

3. That the eruption may be purely hæmorrhagic and not inflammatory (Janowsky).

4. That a systemic poisoning is not a necessary coincident.

The conclusion is drawn that many of these localised eruptions of Group II

nerve-influence in the production of erythemas from drug action. The assertion made many years ago by Wilson, that "the influence of the vaso-motors is involved in the production of roseolas," may be extended to embrace all cutaneous phenomena of a simple congestive character.[1]

The more fugitive forms of drug hyperæmias present many striking analogies both in form and localisation with that large class of eruptions known as mental or emotional congestions, doctor's rash, which is so constant a phenomenon in the examination of nervous females, *erythema pudoris*, &c. These are pure angioneuroses dependent upon an impression emanating from the emotive centres.

Clinical analogies with drug eruptions may also be found in traumatic, septicæmic, diabetic, and menstrual eruptions, the *taches cérébrales*, tabetic ecchymoses, &c., occurring in cerebral and spinal diseases, and which are absolutely inexplicable except on the theory of their neurotic origin.

We have seen that in many cases the severer forms of eruptive disturbance are the outgrowth of the simpler, the grade of the eruptive element depending upon the continuance of the morbid stimulus. There are certain other cases, however, in which the eruption is only developed after the more or less prolonged use of the drug, the struc-

are due to a specific action of the peripheral nervous system in persons of special susceptibility.

It is evident that some of these eruptions could be explained by supposing that the local irritation of the nerves is communicated not only to the peripheral nerve-centres, but to more and more central ones, according to the vulnerability of the subject, so that the noxious influence is reflected and the vascular system disturbed over wider and wider areas, often at a distance from the primary irritation. Even bilateral and symmetrical eruptions might be thus explained. In the third group there is often no dermatitis at the site of application of the drug, or not till there is evidence that the drug has been absorbed.

The author concludes that such drug may act as a simple local irritant, and the extent of the disturbance excited corresponds in great measure with the vulnerability of the subject to the particular drug, and with the importance of the nerve-centre reached by the disturbing influence. Other eruptions are secondary to the absorption of the drug, and are to be classed with those caused by the ingestion of the medicaments.—T. C. F.

[1] See the very interesting appendix on "The Pathogeny of the Erythemata" in the French translation of Kaposi's 'Lectures on Diseases of the Skin,' 1891.—T. C. F.

tural changes having a definite relation to the size and continuance of the dose, such as the severer forms of the bromide and iodide eruptions, for example. The changes in the skin are often associated with the toxic systemic effects of the drug, known as "Iodism," "Bromism." In these cases, not only is there a change in the form of the inflammatory process in the skin, but in addition to the vascular pathological phenomena there are nutritive or trophic modifications depending upon a profound constitutional disturbance.

While there is no doubt that the vaso-motor nerves modify to some extent the nutrition of the tissues to which they are distributed, yet in these severe forms, characterised by a disturbance of local nutrition more or less profound, another agency than vaso-motor innervation is apparently involved—they are probably due to an impression of the drug upon the trophic centres, which regulate nutrition.[1]

Physiological research, as well as pathological facts, have demonstrated that the nervous system exercises a constant and controlling influence upon the nutrition of the tissues. Whether this influence is exerted through the nerves which regulate vascular supply, or whether there exist certain nerves with specialised functions which have been denominated trophic nerves, is immaterial to our present inquiry. The fact remains that a trophic influence is exerted upon the cutaneous tissue by the nerve-centres, and that when any impression disturbs this regulating power, perversions of nutrition result. This disturbing impression may be made upon the nerve-centres or upon the peripheral nerves. Peripheral irritations will cause reflex alterations of nutrition precisely as they cause reflex disturbances of motor functions.

The direct dependence of cutaneous lesions, varying in character and intensity from simple dermatitis to the profoundest changes in the skin and cellular tissue, upon altera-

[1] Du Castel ('Des diverses espèces de Purpura,' Thèse de Paris, 1883) seeks to explain "medicinal purpuras" by the action of a combination of perturbation of the nervous system and alteration of the blood. Brooke (see note, p. 388) seeks to explain how purpura may be part of the hyperæmic process.—T. C. F.

tions in the peripheral and central nerves, has been demonstrated by numerous anatomico-pathological investigations. The neuropathic origin of pemphigus, zoster, leprosy, symmetrical gangrene, decubitus acutus, mal perforans, ulcers of the leg,[1] exfoliative dermatitis, and certain forms of eczema has been thus demonstrated. May we not reasonably infer a like pathogenesis in the case of drugs which are capable of exercising such a profound influence upon the nervous system?

The fact that structural alterations of the nerves, leading in many cases to abolition of their functions, have been found in the diseases just referred to, does not militate against this view. Physiological experiments have proven that molecular changes in the nerves, from excitations of transient influence—electricity, for example—affect the nerve-functions precisely as do gross pathological changes of structure, or even section of the nerve.

While there is no positive evidence that drugs produce modifications of molecular arrangement, however minute, in the nerve tissues, yet it is a noteworthy fact that a large proportion of the medicinal agents which determine eruptive disturbances act specifically upon the nervous system. Many drugs not credited with this physiological action undoubtedly exercise it. Proof of this proposition is found in the neuropathic character of the several groups of symptoms comprehended under the general terms "iodism," "bromism," "cinchonism," "hydrargyrism," &c., with which the irritant action of the drugs upon the cutaneous surface is so often associated.[2] All authorities recognise these manifestations as due to a disorder of the central nervous system, caused by the depressant action of the drug upon the brain and spinal cord. If the impairment of sensation of mucous membranes, formications, muscular tremors, troubles of intelligence, paretic phenomena, and other grave symptoms of "bromism" be manifestations of the effects of

[1] Ulceration in syringo-myelia, vesicular and bullous eruption, and "glossy skin" in irritative lesions of peripheral nerves, &c.—T. C. F.

[2] Our knowledge of the production of multiple neuritis from various intoxications (organic and inorganic) has much increased in recent years.—T. C. F.

the drug upon the nerve-centres, why is not the concomitant "bromic acne," with which these symptoms stand in intimate connection, likewise a neurotic phenomenon? It is irrational to separate the skin affection from the group of other symptoms which make up this clinical picture, and assign to it an entirely different pathogenesis.

The only correct interpretation of the physiological predisposition, known as idiosyncrasy, as a determining cause of drug eruptions is based upon a recognition of their neurotic character.

We may safely assert that so far as we can apprehend the nature of idiosyncrasy, as affecting the cutaneous action of certain drugs, it seems to depend upon a heightened susceptibility of the nervous system, associated or not with a specific predisposition of the cutaneous tissues to irritant impressions. In persons who manifest this idiosyncratic intolerance, the equilibrium existing between the skin and the nervous system in their vascular and nutritive relations is easily disturbed, the form and intensity of the resulting reaction being largely determined by the physiological properties of the tissues affected.

As is well known, the incidental effects of drugs may be manifest in other organs. The explanation of their more frequent determination toward the skin must be sought for in the sympathetic lines which unite the nervous and cutaneous systems. The skin is not only the receptive surface of all sensory modifications from the external world, but it is the principal medium through which the nervous system manifests its emotional and other disturbances.

Proof of the neurotic character of drug eruptions may also be drawn from the alterations of sensibility with which they are associated; their symmetry; their generalisation or their restriction to certain regions, according as the drug affects the general nervous system or the special nerve-centres which preside over particular cutaneous departments. Indeed, their very caprices and contradictions constitute a strong proof of their neurotic origin, suggesting a modification of the controlling, regulating influence exercised by the nerves upon circulation and nutrition.

## DIAGNOSIS.

The diagnosis of the eruptions caused by the *external* use of drugs, whether from accidental contact, or intentionally applied for therapeutic purposes, is generally easy. The limitation of the irritation to the parts exposed to direct contact,[1] which is commonly the case, and a knowledge of the specific forms of skin irritation which certain drugs almost invariably produce, is sufficient for a diagnosis. The black comedo-like points which characterise tar acne, for example, are pathognomonic. The peculiar staining of the hair and nails caused by chrysophanic acid would at once suggest the explanation of a coincident inflammation of the skin. The pustules produced by croton oil and tartarised antimony present certain characteristics by which they can be differentiated from each other, and from other pustular lesions which have a different mode of origin.

The eruptions caused by the *internal* use of certain drugs derive their chief clinical importance from their resemblance to the eruptive fevers and idiopathic affections of the skin.[2] The exanthem of quinine and belladonna bears a close resemblance to the rash of scarlatina, and when it is accompanied with fever and elevated temperature the simulation is so perfect as to deceive the most skilful and practised

[1] It has already been pointed out that not infrequently these limits are overstepped, and a more or less generalised eruption may ensue. This fact will be found illustrated later on.—T. C. F.

[2] And to the exanthematic outbreaks which are associated with various toxæmiæ, *e.g.* "surgical eruptions," "vaccination rashes," outbursts occurring in the course of Bright's disease, &c. Crocker justly remarks that "whilst there are many forms of eruption due to drugs, only two—iodine and bromine, and their salts—are capable of exciting lesions which are special and peculiar. In all the rest the eruption itself follows a recognised type, and it is only from the circumstances under which it occurs that the cause is ascertainable."

The sudden onset of an angioneurotic eruption (scarlatiniform, morbilliform, roseolar, urticarial, like erythema multiforme, vesicular, bullous, or purpuric) during the administration of a drug should always excite suspicion.—T. C. F.

observer. The copaiba eruption may resemble that of measles; this similitude is heightened by the irritant effects of the drug upon the mucous surfaces, causing redness of the conjunctivæ, congestion of the throat, &c. Certain forms of iodic eruption may simulate both smallpox and syphilis; other examples will be noted in considering the clinical features of the different drug eruptions.

It seems hardly necessary to suggest to the practised physician that, when cutaneous symptoms appear which present points of dissimilarity with the clinical features of ordinary eruptions, he should make careful inquiry as to what drugs the patient has been taking.

The elements upon which a diagnosis is based relate, not only to the characters of the eruptive form, but its sudden development, usually without fever or severe constitutional disturbance, its distribution, and its rapid disappearance upon cessation of the action of the exciting cause. As before intimated, the prompt return to a normal state of the skin, so soon as the offending drug is withheld, constitutes the distinctive differential sign of drug eruptions.

The offending agent may occasionally be revealed by its presence in the physiological secretions. As most drugs are usually eliminated by the kidneys, and a few in part by the salivary and sweat glands, the presence of the drug may be detected in the urine, sweat, or saliva.

The most approved tests for the detection of the offending agent in the urine will be considered in connection with each particular drug. Many of the recorded tests are applicable only when the drug has been taken in toxic doses, or when its use has been long continued, leading, presumably, to a considerable accumulation in the system. But it must be borne in mind that in many cases eruptive disturbances of the skin are occasioned by small or indifferent doses. For the detection of such minute quantities, the rough tests generally recommended are altogether inadequate, and processes much more refined and delicate must be employed, otherwise the examination of the urine would lead to results which are only misleading and deceptive.

Many drugs undergo such marked modifications in the economy, in the process of absorption and elimination, that

their morphological identity is entirely destroyed, and, obviously enough, no satisfactory tests can be given for their detection in the excretions.

The sense of smell is often alone sufficient to detect the presence of turpentine and other essential oils in the urine without resort to troublesome tests.

Again, the peculiar and characteristic odour exhaled by the patient who has been taking certain drugs, such as the balsamics, may afford convincing proof of the nature of the exciting cause.

The greyish-brown discoloration of the skin from the prolonged use of arsenic, the slaty-gray pigmentation caused by nitrate of silver, could hardly be mistaken.

There are many other important diagnostic distinctions to be drawn from the character of the eruption as a whole —its configuration, grouping, the parts affected, its course, &c.—which are of much more significance than the elementary lesions.

It is important to bear in mind, however, that in many cases the clinical features of drug eruptions have nothing distinctive, nothing definite, nothing fixed. They are as varied in their manifestations as are the physiological peculiarities of the individual in whom they develop; neither in their mode of invasion, their eruptive elements, nor in their subjective symptoms can they be distinguished from eruptions of constitutional origin.

## TREATMENT—PROPHYLAXIS.

In the immense majority of cases of eruptions, caused by either the external or internal use of drugs, the treatment is simple and promptly efficacious. Suppress the cause, the accidents will cease to appear. In exceptional cases the effect on the skin in the shape of new lesions still continues to be manifested for a short time after the discontinuance of the drug, depending, possibly, upon interference with its elimination by the usual channels, and its longer retention in the system. Again, the morbid impress upon the skin may be perpetuated by a diathetic condition, and in the

severer forms by some general cachexia, or local debility of the cutaneous tissues, which retards the prompt return to a normal condition.

But in general it may be said that, no matter how marked the cachexia or how grave the systemic complications present, the eruption begins to improve upon cessation of the use of the drug. As before intimated, this tendency to spontaneous recovery is a constant and invariable feature of drug eruptions, and constitutes an important differential sign, which distinguishes them from the skin affections of constitutional origin.

In certain cases, in which the requirements of the patient's condition may demand a continuance of the use of the drug, notwithstanding its irritating effect upon the skin, the expedient of diminishing or increasing the dose does not apparently modify its untoward effects. In a majority of cases, patients who manifest this idiosyncratic intolerance cannot take the drug in *any* dose without this coincident liability to eruptive disturbance. It has been claimed, however, that the irritating influence of many drugs may be counteracted or held in abeyance by a combination with certain other drugs which act as corrigents, suppressing the cutaneous irritation without defeating the therapeutic object in view. For example, hydrobromic acid is said to counteract the untoward effects of quinine.

Arsenic given in combination with iodide of potassium will, it is claimed, prevent the characteristic acneiform eruption. Sulphide of calcium, belladonna, sulphaniline, &c., are said to exert a similar corrective action. Many other expedients for counteracting the morbid determination of drug action towards the skin will be considered in connection with the study of particular drugs.

It must be confessed, however, that these assertions rest upon a very slender support of clinical observation, and must be regarded in the main as *post hoc* conclusions.

It may be accepted as a fact, definitely demonstrated by clinical experience, that medicines which stimulate the functional activity of the kidneys, thus increasing their eliminating capacity, exert a marked modifying influence upon the tendency of many drugs to cause cutaneous irritation. The

administration of iodide of potassium in large quantities of Vichy, soda-water, milk, or other diluents is to be recommended on this account.

The free use of diuretics will be found serviceable in abating the intensity and hastening the involution of many eruptions caused by the internal use of drugs.

Unna has lately recommended as a prophylactic measure against the toxic effects of pyrogallol, chrysarobin, sulphur, and other reducing agents the free use of mineral acids, with the view of diminishing the alkalinity of the blood. He prescribes during the administration of these drugs dilute hydrochloric acid, fifteen to thirty drops a day. Should toxic symptoms develop, the dose is increased to five to ten grams a day. He has never observed bad results from this method.

*The local treatment* of drug eruptions will vary according to the degree of inflammation present, the extent and severity of the lesions, and the intensity of the subjective symptoms.

Persons whose occupation brings them in contact with irritating substances, as workmen employed in drug manufactories, should change their vocation, or else use measures to thoroughly protect the exposed parts.

The treatment of the simpler forms of drug dermatitis should be essentially palliative; soothing and protective measures should be alone employed. For the relief of the distressing sensations of burning and itching, which are so often a prominent feature, the use of hot baths, medicated with soda or borax, followed by the free dusting of the surface with an inert powder, will be found beneficial. For this purpose, powdered talc, lycopodium, fuller's-earth, or the following—Pulv. Zinci, ʒij; Pulv. Camphoræ, ʒss; Pulv. Amyli, ʒv, M.—are as good as any. A Turkish bath, when available, constitutes the most promptly efficacious means we possess for the relief of pruritus. The use of antipruritics in the form of a spray, as carbolic acid, ʒij—iv; glycerin, ℥ss, to water, 1 pint, painting the surface with a solution of cocain (2 per cent.), or of menthol (grs. ij—x to the ounce); lotions of lead and opium, the black wash, grindelia robusta (ʒi—ij to ℥iv of water), &c., are recommended.

Bland ointments, as Ung. Zinci Benzoati, Ung. Diachyli, or an ointment of oleate of bismuth prepared after the following formula—Bismuthi Ox., ʒj ; Acidum Oleici, ʒvij ; Cera Alb., ʒiij ; Vaselinum, ʒix ; Ol. Rosæ, gtt. ij, M. ; or, when the skin is not broken, an ointment of chloral and camphor (āā ʒss—ʒj to ℥j of vaseline) may be employed.

In the treatment of the severer forms of pustular and ulcerative lesions the use of powdered iodoform or dressings of carbolised vaseline will be found to hasten the reparative process.

In the treatment of furuncular lesions the continuous application of camphorated oil is serviceable in relieving pain and promoting resolution.

### ACIDUM BENZOICUM—SODII BENZOAS.

Friar's balsam, which is but another form of the comp. tincture of benzoin,[1] is credited with the production of eruptive phenomena. Fox reports a case of a very extensive eruption of purpura urticans in a patient who had been directed to inhale the vapour of Friar's balsam two or three times a day. The eruption was confluent upon the trunk, more discrete and urticaria-like upon the extremities. Fox says that the rash may result from reflex disturbance or from the presence of the drug in the cutaneous capillaries; the latter he thinks probable from the strong odour of the drug exhaled.

Benzoic acid, upon the presence of which the virtues of the balsam chiefly depend, is irritant to both cutaneous and mucous surfaces.

Vanini observed in a patient, for whom he had ordered small doses of benzoic acid, a maculo-papular eruption develop on the fourth day. The skin of the trunk became covered with an eruption composed in part of somewhat pale, rose-coloured macules of irregular form and extent, and in part of bright red papules, from the size of a poppy seed to that of a grain of millet. In some places the papules were distinctly discrete, while in others they were notably

[1] Friar's balsam contains the balsamic resin benzoin, storax, balsam of Tolu, and Socotrine aloes.—T. C. F.

confluent, giving to the skin a uniform raised aspect. Around the papules and the erythematous spots the skin presented a normal colour.

The following day, under continued use of the drug, the eruption extended to the face, neck, upper and lower extremities; only the surface of the thighs remained free. The use of the medicine was now suspended, and on the fourth day the macules had faded, the papular element disappearing in about ten days without treatment.

Rohe reports two cases in which the internal use of benzoate of soda in medicinal doses caused eruptive disturbance. The rash was erythematous, with well-defined borders, and was attended with considerable itching. The eruption disappeared, with slight desquamation, upon discontinuance of the drug. It was redeveloped several times by a repetition of the use of the drug.[1]

### ACIDUM BORACICUM—SODII BORAS.

According to Stillé, the long-continued use of borax sometimes produces an impetiginous eruption of the skin.

Modadewko[2] reports two cases in which a 5 per cent. solution of boracic acid, used for washing out the pleural cavity, occasioned an erythematous rash over the face, trunk, and extremities.

Bruzelius saw a wide-spread erythema make its appearance after a few days' use of a 4 per cent. solution of boracic acid taken as an injection[3] in chronic diarrhœa. The eruption was confluent about the neck, and well developed over the body.

[1] Hampeln gave, in twenty hours, three grammes of benzoate of sodium to a boy, aged eight years, for pultaceous amygdalitis. A diffuse scarlatiniform exanthem appeared on the neck, trunk, and arms, and reappeared in a patchy form on the readministration of the drug. Ehrenhaus is quoted as having seen erythema and purpura.—T. C. F.

[2] ? Molodenkow, quoted in 'Lancet,' May 6th, 1882. A pleural and a lumbar abscess-cavity were each washed out for an hour, and "the next evening erythema appeared on the face, and spread on the third day to the neck, chest and abdomen, then on to the thighs, small vesicles appeared on the face and throat, the sight became dim, and both patients died, conscious to the last, one on the fourth, the other on the third day."—T. C. F.

[3] Two pints *per rectum*.—T. C. F.

Gowers reports three cases in which borax administered for a long period to epileptics determined an eruption perfectly characteristic of psoriasis. Scaly patches of variable dimensions, some of them three quarters of a centimetre in diameter, occupied the trunk and limbs, especially the upper extremities, and were spread over both extensor and flexor surfaces; the face was not invaded. The aspect of the eruption was quite characteristic of psoriasis, although there was less thickness of the scales than in spontaneous psoriasis. In two of the cases the addition of a small quantity of arsenic to the borax caused the rapid disappearance of the eruption.[1]

Johnson reports a case in which the injection of 3·6 grams of boric acid was followed by headache, fever, injection of the conjunctivæ, and the appearance of an eruption consisting of a bright erythematous redness, papules, and bullæ. The eruption was localised on the extensor surfaces of the limbs and around the articulations, and disappeared within four days. The acid was readily detected in the urine. In a number of experiments with the application of boric acid in the form of an ointment to the skin, the urine became promptly charged with the borate.

### *Tests for Boric Acid and Borax.*

When notable quantities of boric acid or borax are present in the urine, they may be detected by evaporating the urine, previously rendered alkaline by soda, to a small bulk, then acidulating (slightly) with hydrochloric acid, and dipping into it one half of a strip of turmeric paper; the latter, when dried upon a watch-glass at 212° F., will exhibit a peculiar red colour upon the immersed portion. If this is then

[1] Liveing confirms the observation of Gowers.

Alexander (quoted by Crocker) described a diffuse, erythematous, morbilliform eruption following the administration of "tartarus boraxatus" in large doses for two weeks. Welch records cases of poisoning from packing the upper third of the vagina with boric acid. Burning of the skin, especially of the face, hands, and feet, followed in one case; the skin swelled and looked charred, and subsequently exfoliated. In another case there was severe collapse, and after a week desquamation of the skin.

Féré and Lamy record two cases of an eczematous eruption provoked by the ingestion of borax.—T. C. F.

moistened with a solution of a caustic alkali or alkali carbonate, the colour changes to bluish black or greenish black. But a little dilute hydrochloric acid immediately restores the previous tint.

If the urine is rendered alkaline by soda, then evaporated to a syrup, the latter mixed with a proper quantity of pure white sand and then evaporated to dryness, the residue powdered, covered with alcohol, and concentrated sulphuric acid added, on igniting the alcohol this will burn with a green or green-bordered flame.

### ACIDUM CARBOLICUM.

The irritating effect of carbolic acid directly applied to the skin varies from a slight erythema to complete destruction of the tissues, depending upon the strength of the preparation used and the duration of its contact. The application of strong carbolic acid to the skin causes a painful burning sensation, less pronounced, however, than in the case of other caustics; the affected tissues become white, their vitality is destroyed, and a slough is formed.

Abundant opportunity has been afforded for the study of the effects of weak solutions of this agent upon the skin by the general employment of carbolised dressings in the antiseptic treatment of wounds. The most common eruptive form is an erythema which is especially manifest upon regions where the skin is fine and delicate. The inflammatory reaction may result in the formation of vesicles resembling eczema. Strong solutions of carbolic acid may cause gangrene of the skin, which is usually limited to the region of application.

The use of this agent in the form of a spray no doubt facilitates its rapid absorption through the skin by the minute subdivision of the particles. Irritation of the skin may appear on parts not subjected to the action of the spray from absorption.

Similar effects may follow the introduction of carbolised preparations in abscesses and in cavities lined with mucous membrane, as the vagina and rectum.

The cutaneous effects of carbolic acid poisoning are usually

accompanied with nausea, headache, vomiting, and diminution in the quantity of urine voided. The urine becomes of a dark olive colour.

Koster-Syke reports a remarkable idiosyncrasy against carbolic acid in his own person; and his susceptibility was so marked that merely handling a vessel containing carbolic acid sufficed to develop the outbreak of an eczematous eruption.

Zeissl reports a case of erythema urticatum following the application of Lister's bandage. The eruption appeared upon the back, sides, and extremities in the form of an erythematous redness, studded with artificial wheals. The eruption subsided when the carbolic acid dressing was withdrawn.

Browne reports two cases of carbolic rash under his care resulting from antiseptic dressings. The eruption was of a bright scarlet, which commenced about the edges of the wound, spread over the contiguous surfaces, and became generalised. The eruption was followed by desquamation and some albumen in the urine, resembling in many particulars scarlatina, for which it was at first mistaken.

Dreyfuss observed, as the result of phenic acid dressings to the wonnds caused by circumcision in two Jewish infants, a generalised erythematous eruption accompanied with abundant perspiration and hyperæmia. There was also a tendency to the formation of furuncles lasting several weeks thereafter.

In a case of poisoning from drinking impure carbolic acid treated by Penasse, he observed in conjunction with other toxic symptoms an eruption, preceded by violent itching, papular in character, situated upon the arms and anterior superior region of the trunk.

Rose reports the occurrence of gangrene of the finger from the application of a strong carbolised cotton dressing. This result may possibly have been due to interference with the circulation from compression, as similar results have been observed from simple collodion dressings to the fingers.[1]

[1] It has been stated that warts, which may degenerate into epithelioma, are commonly produced amongst those employed in the manufacture of carbolic acid, but this has been denied.—T. C. F.

*Tests for Carbolic Acid.*

Normal urine contains small quantities of phenol-sulphuric acid, which does not readily respond to reagents until it has been split up into free phenol and sulphuric acid by boiling the urine with hydrochloric acid.

Urine containing notable quantities of carbolic acid has often a dark colour, particularly when the drug has been absorbed from external application.

It may be detected in the following manner.

1. Place into a test-tube about two grains of chlorate of potassium, pour upon it about one half a fluid drachm of hydrochloric acid, and allow the reaction to proceed for about one minute. Then dilute with about three fluid drachms of the urine. Now carefully pour down, along the inner side of the test-tube, a little water of ammonia, so that this will form a layer on the liquid contained in the test-tube. If any carbolic acid is present there will be a coloured ring—varying from faint rose-red to dark brown—at the line of contact of the two liquids.

2. Or mix the urine with one fourth its volume of water of ammonia, then add a little solution of chloride of lime (1 in 20), and warm gently. A fine blue colour, more or less deep, will make its appearance.

The *treatment* consists in suppression of the exciting cause. When the cutaneous effects of the drug are accompanied with symptoms of general phenic intoxication, diuretics should be given to hasten the elimination of the drug. Sulphate of soda internally, as recommended by Baumann and Sonnersburg, injections of atropine, and vigorous frictions are probably the best measures for overcoming the toxic effects.

ACIDUM CHRYSOPHANICUM—CHRYSAROBIN.

Araroba or Goa powder, from which chrysarobin is principally derived, is extremely irritating to the skin and mucous surfaces. Workmen employed in cutting up and pounding the wood from which the powder is obtained are

compelled to protect their hands, eyes, and throat against the irritating dust.

The application of chrysophanic acid to the skin causes an irritation which varies with the strength of the application and the susceptibility of the patient. The effect of the irritation is by no means limited to the seat of application, as in the case of most external irritants, but may extend over a considerable contiguous surface, or may leap to a cutaneous area some distance removed. Chrysophanic conjunctivitis not infrequently follows the application of this agent in the treatment of parasitic diseases of the scalp.

The following forms of inflammatory disturbance may be described:

1. *A Hyperæmia with a Peculiar Purplish or Prune-juice Discoloration of the Skin*, which is quite persistent.

2. *An Erythematous Eruption.*—This may appear as a slight erythematous halo around the points of application, or the congestive redness may become intensified with tumefaction of the tissues, and take on the characters of a general dermatitis. It usually disappears with a slight desquamation.

3. *A Papular Eruption.*—The inflammation may manifest itself as pin-head sized, reddish-brown, firm papules, some of which may become vesicular and pustular; according to Kaposi, who first described this eruptive form, they correspond to the openings of the follicles. This drug has also the property of irritating the sebaceous glands, producing a chrysarobin acne, with a tendency to the formation of nodules rather than of papules or pustules. As in tar acne, each lesion has a black point in the centre.

Farquharson reports a case in which the application of an ointment of chrysophanic acid to a patch of tinea tonsurans caused a dusky red condition of the entire scalp. From the scalp the inflammation extended to the face, which was covered with very minute papules, thickly studded over perfectly normal skin, and attended with a good deal of itching. The eruption disappeared on leaving off the ointment.

4. *A Pustular and Furuncular Eruption.*—This form of eruption is by no means uncommon. The pustules and furuncles are hard and painful, and suppurate slowly. I

have reported a case of tinea barbæ coming under my care in which the application of an ointment (twenty grains to the ounce) produced a number of large inflammatory nodules, with much infiltration and congestion, resulting in a hard, brawny condition of the sides of the face and neck, and which persisted for two or three weeks. Brocq observed a man dying at the St. Louis Hospital, with the most intense general erythema accompanied by symptoms of severe poisoning from chrysophanic acid. He also saw, in the service of M. Vidal, a case of general exfoliative dermatitis of two months' duration, which had been occasioned in the same way.

An erysipelatous condition[1] has been observed in connection with the use of this drug. It most usually affects the head and face with considerable swelling and puffiness of the tissues, sometimes leading to closure of the eyes. The genitals, as well as the face, are specially liable to the irritant action of the drug. It would seem that these irritating effects depend less upon the strength of the preparation than upon the susceptibility of the skin of the individual to irritant action. In a number of cases which have come under my observation an intense dermatitis has been developed by the use of a comparatively mild ointment (5 grs. to ʒj). In two of these cases there was exfoliation of the epidermis in large flakes, as in exfoliative dermatitis. These irritant effects from mild applications are specially liable to occur in women and children, particularly blondes, with fine delicate skins, and render the employment of the agent in any strength impossible.

*Tests for Chrysarobin and Chrysophanic Acid.*

Chrysarobin appears in the urine either as such or as chrysophanic acid.

It may be detected by adding to the urine—concentrated if necessary—a little caustic potassa. If this produces a reddish or red tint, chrysophanic acid is present. If the tint is rendered deeper by blowing air through the liquid, or if it only makes its appearance after the passage of a

[1] An erysipelas-like condition.—T. C. F.

current of air, chrysarobin was present. It is only when this has been converted into chrysophanic acid by contact with air, in solution, that the colour is developed.

### ACIDUM NITRICUM.

According to Stillé, a fine pustular eruption sometimes appears upon the skin after the internal use of nitric acid in medicinal doses.

Bazin found, after two or three frictions with a dilution of nitric acid, that the skin presented a diffuse redness, over which were scattered small solid elevations; after the fourth friction these little elevations became pustules, which soon gave place to small ulcerations, extremely superficial, presenting a blackish point at the centre, and a whitish zone of pseudo-membranous aspect at the periphery, which was surrounded by an inflammatory areola. As the eruption disappeared, small epidermic scales were seen disseminated over the patches.

### ACIDUM PYROGALLICUM—PYROGALLOL.

The topical application of pyrogallic acid may occasion irritation of the skin of varying degrees of severity, from a slight dermatitis to a destruction of the skin, followed by ulceration and sloughing. According to Jarisch, who first introduced the drug to the notice of the profession, it excites localised inflammation, which may lead to epidermic desquamation and the formation of vesicles. This is specially liable to occur on the extremities.

Its most common and characteristic incidental effect upon the skin is, according to Besnier, the production of an erythemato-vesicular eruption.

Allen reports two cases in which a ten per cent. ointment of pyrogallic acid produced a blackened and charred con-

### ACIDUM PICRICUM.

C. H. Hughes found that in a case of chronic malaria one and a half drachm doses of picrate of ammonium set up an urticaria, and probably was the cause of jaundice. The administration of quinine was also followed by urticaria. Such a case obviously requires confirmation.—T. C. F.

dition of the skin for an inch or more beyond the area of the application, with a dermatitis of the adjacent surface. In one case the charred tissues sloughed off, leaving an ulcerated surface which slowly healed, succeeded by a disfiguring cicatrix.

### *Tests for Pyrogallic Acid.*

When this acid has been absorbed, the urine generally appears dark-coloured, varying from brownish to near black.

When the urine is not loaded with colouring matters, pyrogallic acid may be recognised by its behaviour with iron salts, giving a deep blue colour with ferrous sulphate, and a brownish red with ferric chloride. These tints are, however, comparatively faint when only traces are present, and the blue tint, particularly, will be modified to a sort of muddy green. Additional proof may be obtained by shaking another portion of the urine, rendered alkaline with caustic potassa, for some time in a test-tube. If it becomes darker in tint, pyrogallic acid may be assumed to be present. Or a little hot nitric acid may be allowed to react with a piece of starch in a test-tube, and a few drops of the nitrous acid thereby produced added to the urine, which will be rendered brown if pyrogallic acid was present.

The irritant effects of pyrogallic acid upon the cutaneous surface are often accompanied with symptoms of general poisoning.

In the treatment of the toxic effects of pyrogallic acid, Besnier recommends the inhalation of oxygen and the subcutaneous injections of ether. Unna has suggested the administration of dilute hydrochloric acid as a prophylactic measure.

## ACIDUM SALICYLICUM—SODII SALICYLAS.

Irritation of the cutaneous surface has been frequently observed after both the external and internal use of salicylic acid. Its substitution for carbolic acid as an antiseptic in the treatment of wounds has shown that it is even more irritating than the former agent. Callender has stated that a two per cent. solution tends not only to irritate the

wounds, but to bring out irritable vesicles in their neighbourhood. He observed that an ointment of salicylic acid, one part to twenty, brought out a vesicular eruption, the vesicles containing a clear fluid, the intervening skin much inflamed. The area affected was limited to the surface covered by the dressing. Sir Wm. Jenner records a case where the application of salicylic acid to a burn developed a rash very like that of scarlet fever.

Various forms of eruptive disturbance, erythematous, urticarial, vesicular, petechial, &c., have been observed from the internal use both of salicylic acid and salicylate of sodium.

Farquharson reports a case where the use of the drug produced a peculiar bright, punctate rash with erythematous patches, eventually surmounted by vesicles, accompanied with sore throat and constitutional disturbance suggestive of scarlatina.

Erb observed after several days' use of seven-and-a-half-grain doses of salicylate of sodium, an eruption which was at first regarded as an anomalous form of scarlatina. Upon the face, neck, and body it showed itself as a bright red, confluent exanthem. Upon the arms and legs the redness was more blotchy, without papular elevations. The conjunctiva and mucous surfaces of the throat were intensely reddened. The eruption disappeared within two days after cessation of the drug. Three weeks later a similar eruption was developed by three seven-and-a-half-grain doses of salicylic acid.

Dreschfield observed in the case of a lady an erythematous eruption which was repeatedly developed by the internal use of salicylate of soda. The whole body became covered with an erythematous rash. The face, arms, and legs were very œdematous, and the lips very much swollen. Upon examination of the urine with perchloride of iron, a distinct salicylic acid reaction was obtained. Within a few days the rash and œdema disappeared, and the skin peeled off from the face, legs, and arms in thin flakes. Another patient, suffering from acute articular rheumatism, for which he was ordered fifteen-grain doses of salicylate of sodium three times a day, was soon troubled with a well-marked urticaria.

A second attack of urticaria was promptly developed upon resuming the use of the drug. He also reports a case of skin eruption very closely resembling erythema nodosum, following the use of a vaginal wash containing salicylic acid. On a previous occasion salicylate of sodium, taken internally by the same patient, had produced an eruption of similar character.

Parsons saw in the case of a lady who was taking small doses of salicylate of soda a rash resembling measles upon the face, hands, arms, and body. The rash disappeared upon discontinuance of the drug, and reappeared when its use was resumed.

Heinlein observed from the use of four 3j doses of salicylate of sodium a diffused redness of the left half of the face, the lower extremities, and the right side of the chest, with slight œdema of both eyelids, the upper lip, and the legs as far as the middle of the thighs.[1] These symptoms promptly disappeared with the cessation of the medicine. After a remission of several days a drachm dose was administered; half an hour afterward there appeared a diffuse erythematous redness over the greater portion of the body, while a profuse eruption of wheals was observed over the abdomen and lower extremities, with considerable œdema of the face. The urticarial phenomena disappeared in the course of an hour or two, the erythema by the next day.

Leube also saw an eruption of urticarial wheals follow the use of a drachm dose of salicylate of sodium.[2]

Wheeler reports a case where the drug produced an eruption of vesicles and pustules upon both upper and lower extremities, accompanied with profuse perspiration. It disappeared on stopping the medicine.

Rathery says, "Every time I have occasion to use salicylate of sodium in my own person, my hands and body are covered with a pemphigoid eruption."

Cavafy reports a peculiar eruption from the use of sali-

[1] Albuminuria was induced, and this symptom is recorded in conjunction with the eruption by Leube and Freudenberg.—T. C. F.

[2] Leloir observed a giant urticaria accompanied by plantar and palmar nodosities simulating pseudo-rheumatic nodosities.—T. C. F.

cylate of sodium. It consisted of erythematous patches which became covered with vesicles, some very minute, others larger and confluent, while others were grouped, resembling herpes.

Freudenberg saw, after five-grain doses of salicylic acid taken daily for five days, a petechial eruption in which some of the petechiæ were as large as a half-dollar; other extravasations occurred in the shape of vibices. They first appeared on the back, but spread the following day over breast, arms, shoulders, hips, and thighs. The spots became pale in the course of a week, and the epidermis was exfoliated in great scales from the affected parts. Second experiments in the same patient produced a similar result.

Rosenberg observed an eruption of purplish spots all over the body of a patient from the use of salicylic acid. The medicine was discontinued, but upon another trial a month later, in addition to the purpuric eruption, there appeared a number of blebs filled with serum, situated on the back and extremities, and also upon the conjunctiva and mucous membrane of the tongue and lower lips. A third trial of the medicine resulted in a precisely similar eruption.

Watelet reports two cases of rheumatism treated with salicylic acid, in which the drug occasioned coldness of the extremities, and in one case gangrene of the lower extremities.

The erythematous eruption produced by salicylic acid and its salts bears a striking resemblance to that of antipyrin, belladonna, chloral, &c. The rise of temperature, sweating, œdema, with which the erythema is usually accompanied, are undoubtedly vaso-motor phenomena. Experiments upon animals have shown that the salicylates act primarily and principally upon the vaso-motor centres.

### *Tests for Salicylic Acid and Salicylates.*

On adding to the urine a little solution of ferric chloride, there will at first appear a flocculent precipitate of phosphate of iron; but on further addition of the reagent the liquid will assume a more or less intense violet colour.

If there is doubt, concentrate the urine to a small bulk,

acidulate it with hydrochloric acid, then shake it with a mixture of equal parts of chloroform and ether. Evaporate the latter after separation, and apply the above test to the residue.

### ACIDUM TANNICUM.

It is well known that tannic acid exerts an influence upon the functions of the skin, notably diminishing the insensible perspiration.

The sole reference which I have found in medical literature relating to the irritant effects of tannic acid upon the skin is that of Dr. Williamson. He records the case of a lady in whom an erythematous eruption, affecting the face and neck, was developed three separate times by the use of tannic acid. Tannin injected into the rectum, tannin accidentally inhaled, the ingestion of an infusion of uva ursi leaves, which contain 35 per cent. of tannin, were all followed by identical symptoms. An interesting fact in this connection was that gallic acid, taken internally, produced no untoward symptoms.

Gallic acid passes off through the kidneys unchanged within one hour after its ingestion. Tannic acid is converted into gallic or pyrogallic acid before excretion.[1]

### ACONITUM.

This drug, as is well known, exerts a marked influence upon the cutaneous system.

The external application of aconite to the skin causes first a sensation of tingling and then numbness, from the paralysing action of the drug upon the sensory nerves. Congestion, redness, and an eruption of itchy vesicles have also been observed, and according to Dierbach, quoted by Piffard, it may produce an erysipelatous inflammation.

Many writers on materia medica speak of an irritable vesicular eruption, which frequently follows the internal

[1] Lange saw tannic acid applied to the pharynx produce serious œdema of the larynx, a general urticaria, and marked prostration. Schramm also observed œdematous swelling of the nose and general urticaria follow the use of a 1 to 300 tannic acid nasal douche.—T. C. F.

use of aconite. It is attended with a sense of formication and excessive itching. Pustules and blebs have also been observed.

### AMYGDALA AMARA.

Phillips says that an eruption resembling urticaria often comes out on the skin after the ingestion of this drug.

Gregory noticed such an eruption upon himself after eating a bitter almond. The same effects may follow the use of bitter almond and cherry-laurel water, depending no doubt upon the hydrocyanic acid present in both preparations.

Rayer observed from the use of frictions with *l'huile de laurier-cerise* an extensive patch of erythema over the loins, nine by six inches in extent. The exanthem consisted of a large non-elevated, red patch, the redness not uniform, the skin appearing as if spotted and discoloured at certain points. The red spots gradually became paler, followed by desquamation on the seventh day.

### ANACARDIUM.[2]

The oil of the cashew nut is extremely irritant when applied to the skin, producing dermatitis and erysipelas. The effect is not limited to the parts with which it comes in direct contact, extensive inflammatory disturbance being observed upon parts distant from the point of application. Œdema and eczematous inflammation of the face have been observed.

### ALCOHOL.

Nevins Hyde reports a case of urticaria from alcohol. G. Kaempfer saw, in a man suffering from articular rheumatism who had been a heavy drinker, a transient erythema appear half an hour after taking brandy, whisky, beer, &c., but not after absolute alcohol. There was hyperæmia of the retinal vessels, and a scarlatina-like pharynx.—T. C. F.

[1] I find references to *A. orientale*, or the Malacca bean tree, *A.* or *Cassuvium occidentale*, or the cashew of the English and the acajou of the Indians, and *Semecarpus anacardium*. Burnett, in his 'Outlines of Botany,' London, 1835, refers to the irritating black varnishes made from Semecarpus, &c., and widely used in India, China, Burmah, &c. The action of these varnishes seems to be identical with "lacquer" poisoning.—T. C. F.

Stickney noted, from its local application, pain, itching, red papules changing to pustules, crusts, and desquamation.

According to Bazin, the oil, when applied to the skin, sometimes produces vesicles which rapidly become purulent.

Schwerin reports a case of a woman who had put one half of a bean in her ear to relieve toothache and pain in the face. A violent erysipelas resulted. The face was bloated, both eyelids infiltrated, and the ear, cheek, and front of the neck reddened and swollen. The external auditory canal, the external ear, and the adjacent surfaces were covered with vesicles.

In another case, also quoted by Lewin, an anacardium bean, divided longitudinally, was placed upon a string hung around the neck in such a manner that it lay over the manubrium sterni. Two days later an erysipelas had developed, extending over the whole front of the chest, the mammæ, the region of the shoulder as far up as the lower jaw, and presenting a number of vesicles upon its surface.

Hughes states that, taken internally, anacardium has a remarkable influence upon the skin. In its slightest degree of action it causes the appearance of wheals like those of urticaria tuberosa, with itching, burning, and swelling, terminating in desquamation. When operating more intensely it develops eczematous vesicles, and even bullæ.

It is claimed that the irritating effects which are so often observed from the use of preparations of vanilla are due to the oil of cashew, with which the vanilla pods are coated before being sent to market.[1]

[1] J. C. White gives illustrations of the irritative qualities of *Semecarpus anacardium* (cashew nut). Its active principle is a yellowish oil called cardol.—T. C. F.

### ANILINE—ACETANILIDE (ANTIFEBRIN).

The effects arising from the local application of the numerous aniline dyes are considered under arsenic. Acetanilide (antifebrin) is aniline in which an atom of hydrogen is replaced by the radical acetyl. Many cases are reported in which toxic effects have been caused, often associated with cyanosis; and Morehouse records an eruption which I have been unable to refer to.—T. C. F.

ANTIMONIUM—ANTIMONII ET POTASSII TARTRAS.

The external application of tartarised antimony to the skin excites a very characteristic eruption, which in its course, and the anatomical form of its lesions, resembles the eruption of variola. Its contact produces a hyperæmia, then papules which are converted into vesicles, which later develop into pustules. The pustules mature about the fifth day, desiccate, and form scabs, which often leave, on falling, indelible cicatrices. Sometimes it produces large ecthymatous ulcers, with deep sloughs and extensive loss of tissue, resulting in permanent disfiguration. Jacobi, of Wurzburg, reports a case in which there was destruction of the bony tissue, the application of antimonial ointment to the scalp causing a perforation of both tables of the parietal bone. Applied on distant parts of the body, it may cause eruptions on the genitals or around the anus, without direct contact. Pustular eruptions not infrequently develop secondarily on the genital parts several days after inunction with tartarised antimony, without there having been, so far as could be ascertained, a transference of the drug to these parts from the original point of application. This would seem to be due to the absorption of the drug and its presence in the circulation.

Opinion is divided as to whether the effects are due to the irritant action of the drug upon the peripheral nerves leading to inflammatory changes, or to a direct action upon the coats of the vessels themselves from the presence of the drug in the vascular channels.

Trousseau says that the internal administration of tartarised antimony will produce a vesiculo-pustular eruption, like that produced by the salt applied to the skin.

Imbert Gourbeyre cites five cases in which eruptions closely resembling those produced by tartar emetic ointment have appeared during the internal administration of the drug. He also quotes a case where a red eruption occurred over the whole body from a single large dose of antimony. This observation has been duplicated in the experience of others. In other cases urticarial and pustu-

lar eruptions have been observed from the internal use of antimony.

Langston states that, after the administration of tartar emetic for three or four days to his wife, an eruption, consisting of a dense crop of tartar emetic pustules, broke out all over the surface of the upper part of the body, including the arms. The outbreak of the eruption was preceded by an alarming sensation of numbness and tingling.

### *Tests for Antimony and Arsenic.*

Among the various methods available for their detection, the following will probably be the most expeditious in the hands of the physician:

Acidulate the urine strongly with hydrochloric acid in a narrow-mouthed flask; immerse in it a piece of *bright* copper wire or foil, and boil for some time. If, after the urine has boiled down to one half, there is no visible metallic deposit upon the copper, the above two metals may be regarded as absent. If a metallic coating has been produced, this is to be examined as stated below.

Should the urine contain constituents which are coagulated or precipitated by boiling or acidification, they must first be removed.

The coated copper wire or foil is taken out of the flask, washed thoroughly in water, dried, and then heated in a glass tube closed at one end, the further procedure being that laid down in all text-books.

## ANTIPYRIN (ANALGESIN).

Although the introduction of antipyrin as a remedial agent is of comparatively recent date, yet a large number of cases have been reported in which eruptive disturbances have followed its employment.

The eruption of antipyrin is usually erythematous in character. It consists of small, irregularly circular, slightly elevated reddish patches, which may be discrete, or confluent forming large patches resembling the exanthem of rubeola. The redness disappears on pressure, leaving a

brownish pigmentation. The duration of the eruption is rarely more than five days; it is occasionally followed by desquamation. It is frequently attended with profuse sweating, and causes more or less itching. Its seat of predilection is the chest, abdomen, and back, but it may also occur upon the extremities; it affects the extensor rather than the flexor surfaces. The face and upper part of the neck are usually spared. The eruption may exceptionally follow a small single dose of the drug, but ordinarily it is only provoked by a continuous course of antipyrin treatment for several days, although, in a large number of cases experimented upon, the eruption did not occur in the exact period during which the largest quantity of the drug was taken. It begins to subside promptly on the disuse of the drug, and generally, but not always, recurs when the drug is again administered.

Ernst was the first to note the incidental effects of antipyrin upon the skin. He reports five cases in which an eruption resembling measles was developed upon the trunk and extremities, and also upon the palmar and plantar surfaces.

Leube records a case of a "measly eruption" following the employment of antipyrin, which promptly disappeared with the cessation of the use of the drug. Its resumption brought out a uniform scarlet-red eruption over the entire surface of the body, attended with swollen eyelids, injected conjunctivæ, and free lachrymation.

Biermer, reported by Alexander, observed in three cases measly eruptions, and one case in which the use of the drug was always followed by an urticaria.

Frankenberg observed in seven patients, out of a large number submitted to antipyrin treatment, an eruption of reddish, irregularly round spots, the size of a lentil, giving the skin the appearance of a "rose marbling."

In two cases of antipyrin rash reported by Bloomfield the eruption consisted of slightly raised erythematous patches, one eighth to one half inch in diameter, of an Indian red colour, covering the entire body. Here and there were a number of vesicles the size of a No. 6 shot.

Bielschowsky observed, after the use of antipyrin in a

case of typhoid fever, an eruption of hæmorrhagic wheals on the extremities.[1] They followed the subsidence of the typhoid rash, and were succeeded by a scarlatinoid eruption.

Graham reports the occurrence of a patch of purpuric maculæ on the back of a patient who was ordered five powders of antipyrin, twelve grains each.

Strauss reports a case in which moderate doses produced, in conjunction with severe constitutional effects, a purpura-like eruption on the back and limbs.

Draper treated twenty cases of typhoid fever with antipyrin. In six of these cases the drug produced an eruption resembling measles, and in one case, in which large doses were continued for a prolonged period (twenty days), the drug caused a copious erythematous rash, which was followed by an eruption of furuncles. In one case there was a macular eruption of a purpuric character.

The mode of production of the cutaneous effects of antipyrin is to be explained by the action of the drug upon the vaso-motor system of nerves. It causes paralysis of the vaso-motors, which is followed by dilatation of the cutaneous vessels. The largely increased amount of blood present would naturally favour the production of the characteristic erythematous and urticarial eruptions. The hæmorrhagic exudations occasionally observed are probably produced in the same way.[2]

[1] Drasche and Grandclément also record a hæmorrhagic eruption.—T. C. F.

[2] Our enlarged experience shows that eruptions follow the ingestion of antipyrin with considerable frequency, judging from the literature of the subject, and the number of cases I have seen and heard of in London hospitals. Germain-Sée estimated the frequency of its occurrence as 1 in every 12 or 15 women, and 1 in every 50 to 60 men to whom the drug was administered in repeated doses. The morbilliform rash is the usual one, and may be associated with oculo-nasal catarrh. It usually begins on the limbs and spreads to the trunk, but a wide extent of surface may be almost simultaneously affected. There is never much rash on the face. The eruption is brighter than that of measles, less crescentic, and generally disappears quickly when the drug is discontinued or diminished, and more slowly when continued. The eruption tends to run into more or less extensive patches, especially on the extensor aspects of the limbs and trunk, leaving areas of healthy skin. There may be considerable swelling and infiltration. The rash may be limited to the limbs, but is always bilateral. The

### *Tests for Antipyrin.*

Antipyrin may be volatilised when distilled with water. Urine, however, after small doses of antipyrin, does not yield the latter by distillation until after it has been boiled with hydrochloric acid, which fact permits the conclusion that antipyrin is, at least partly, eliminated as a copu-

morbilliform eruption may appear exceptionally after small doses and very quickly.

A scarlatiniform eruption has been recorded by Wilson, Hardy, Spitz, Durand, Tuczek, and others.

Urticaria is of fairly common occurrence, and it is to be noted that, unlike the morbilliform rash, it usually follows very quickly (ten to twenty minutes) the ingestion of the drug, and often arises from single small doses (four to ten grains). It may be provoked again and again, but in Martini's case, where this resulted, there was no eruption on giving a hypodermic injection. The urticaria may be intense and generalised, or scanty and more localised. Dutt records a case in which itching and tingling occurred without eruption.

Several authors mention more or less marked congestive redness of the face, often associated with a similar condition of the conjunctivæ and buccal and respiratory mucous membranes and hypersecretion. There may be very considerable œdema of the eyelids or face. Watkins records a case in which the swelling was limited to the upper lip. Short mentions the case of a man who took five grains of antipyrin on three occasions, and each time suffered from marked flushing of the face, an unpleasant choking sensation in the throat, then redness and swelling of the nose and lips, followed by herpes-like vesicles on the nose, lips, and inside of the cheeks, swelling, redness, and itching of the hands and feet, penis and scrotum, and anal margin. Archer saw a case in which an intense itching was experienced, and bullæ formed in a ring round the anus.

In a case reported by Veiel there occurred, immediately after taking the drug, violent pruritus of the lips, palms, soles, glans, followed by œdema of and formation of bullæ on the lips, and bullæ between the toes and on the palatine vault. On the palms and soles itching, urticated patches formed. Three similar recurrences at intervals were observed.

Petrini observed itching and the formation of bullæ on the face, mouth, neck, shoulders, arms and forearms, trunk, back, breast, abdomen, buttocks, and to a less extent on thighs and legs. This result was probably due to a dose of 3 or 4 grammes, whilst later on a dose of 2 grammes produced only a few bullæ, and one gramme only erythema.

As in the case of other drugs, toxic effects are frequently produced without the occurrence of a rash, but the latter frequently arises without other toxic symptoms. Sometimes intoxication and a rash are co-existent. A spirituous breath may be noticed.

lated compound, probably as antipyrin-sulphuric acid. When much antipyrin has been taken, however, it is found free (probably only in part free) in the urine.

Urine containing free antipyrin, or in which it has been set free by boiling with a little hydrochloric acid (in which latter case the excess of acid should be subsequently neutralised), is rendered red by ferric chloride, and bluish green by nitrite of sodium or by dilute nitrous acid. The latter is best prepared by allowing hot nitric acid to act upon starch, and diluting with a little water.

### ARGENTI NITRAS.

The peculiar discoloration of the skin following the prolonged ingestion of nitrate of silver, which has been variously described as "bluish-grey," "steel-grey colour," "greyish-black," and which is most marked on the face and flexor surfaces, is comprehended under the general term "argyria." It is caused by a deposition of granules of the metal in the tissues, most abundant, according to Neumann, in the papillary layer. Granules are also found in the other layers of the skin, also on the external wall of the hair-follicles, sebaceous glands, and sweat-tubes. I have seen in the case of a young woman under my care for syphilis, who had previously used for several months a solution of nitrate of silver for the relief of an obstinate granular conjunctivitis, a copious deposit of the metal upon the conjunctival mucous membrane which had caused a blackish discoloration, quite noticeable even at a distance.[1]

Charcot observed, after the long-continued ingestion of nitrate of silver, an erythematous and papular eruption attended with pruritus.

Argyria derives a certain clinical importance from the fact that it may be mistaken for Addison's disease.

According to Gamberini, the internal administration of iodide of sodium or potassium, and the long-continued use of warm baths, has proved successful in removing the discoloration of the skin caused by nitrate of silver.[2]

[1] This disfigurement is well known to ophthalmologists.—T. C. F.

[2] I have not attempted to collect the bibliography of argyria, but it will

## ARNICA.[1]

Arnica, which is popularly regarded as a sovereign remedy for contusions, sprains, &c., is often prescribed by the physician under the mistaken impression that, even if it does no good, it can do no harm. Oftentimes, however, the external application of the tincture of arnica, even when largely diluted,[2] is far from proving innocuous and inoffensive.

The strong tincture always exerts a local irritant action when applied to the skin, and in susceptible persons it causes eruptive disturbances of various forms and degrees of severity.[3]

The most common form of arnica dermatitis is an erythemato-vesicular eruption which presents certain analogies with the poison oak eruption. The irritant action of arnica is first manifested by a hyperæmia of the affected surfaces, attended with a sensation of burning and intense itching.

Ordinarily within a few hours there is developed upon the erythematous base an eruption of pin-head sized, reddish papules, intensely itchy, and which soon become converted into miliary or pea-sized vesicles, which may remain discrete, or form, by their fusion, bullæ of considerable size and irregular outline. The walls of the vesicles are usually ruptured by rubbing and scratching, and the exudation dries, forming yellowish or brownish crusts.

be useful to point out that many cases have been recorded in which the characteristic leaden-blue or violet-grey discoloration has followed the application of lunar caustic to the mouth and throat. In such cases the inquirer may be put off the scent by the patient denying the ingestion of any drug. The mucous membranes and other structures may be involved in argyria.

Lewin and Blaschko have written on the localised argyria found in workers in silver. It occurs on exposed parts of the skin in bluish "taches," which are permanent. These taches are due to grains of silver lying in the corium in ramified streaks. Its distribution appears to differ from that found in the so-called "medical argyria."—T. C. F.

[1] The limited literature on the subject of arnica dermatitis is probably no guide to the frequency with which the eruption may occur. The knowledge that arnica occasioned such results was wide-spread, and cases were not recorded. The drug is now comparatively little used.—T. C. F.

[2] And to the unbroken skin.—T. C. F.

[3] Febrile disturbance may be associated with the dermatitis.—T. C. F.

According to White, most cases of arnica dermatitis present a distinctly eczematous type in the development of hyperæmia, papules, vesicles, excoriations, and crusts in regular order, yet many cases have been observed in which the primary immediate effect was the production of large blebs or blisters.

Exceptionally the dermatitis may spread over surfaces remote from the region of original application by transference of the irritative agent by scratching or otherwise.[1]

Fox has observed that the tincture of arnica may produce an erythema and tumefaction of the parts to which it is applied, and even a veritable eczema.

Wilson reports a well-marked eczematous eruption from application of tincture of arnica to a contused shoulder. The whole of the front of the shoulder was of a deep red colour, and presented the character of an eczema vesiculosum et ichorosum, and extending over the whole of the right side of the chest was a crop of pimples of eczema papulosum seu lichenoides, the pimples being large and of a dull red colour; same eruption on thighs, scrotum, head, face, and hands. He refers to numerous cases reported by Professors Galassi and Mazzoni, of Rome, in which the symptoms of the eruption were slightly elevated red puncta, which are quickly converted into middle-sized vesicles similar to those produced by croton oil, swelling and burning heat, and spreading to surrounding parts.

Violent erysipelatous inflammation, even ending in death, has resulted from the application of arnica. Purpuric eruptions have also been recorded.

Farquharson reports a case occurring in Hebra's clinic, in which an acute inflammation of both hands, with huge blisters almost running into gangrene and causing partial destruction to the tissues, was caused by the application of the tincture of arnica. He also records a case coming under his observation in which a weak solution of tinct. arnica caused an erysipelatous inflammation which slowly spread over the entire body.

[1] This spreading dermatitis has been described as erysipelas, and Davidson mentions the formation of abscesses at a considerable distance from the original seat of application of the arnica.—T. C. F.

Laissus reports two cases in which tincture of arnica applied for contusions produced well-marked symptoms of vesicular erysipelas; both patients were females, with fine, sensitive skins.

Paul de Molènes reports four cases, coming under his personal observation, in which compresses of tincture of arnica applied to contusions caused vesicular and phlyctœnular eruptions.

Cartier reports, as a result of the application of tincture of arnica to the face for contusion, an erysipelatous swelling; the face became enormously swollen, closing the eyes; skin bright red and covered with phlyctœnulæ, which discharged abundantly a clear lemon-coloured fluid: the redness extended to the neck, which was occupied by small vesicles; the submaxillary glands were swollen, producing dysphagia; temperature increased, urine scanty, mahogany colour, like that of an icterus patient; although redness and inflammation disappeared under liniment of lime-water and oil, desquamation was not completed for two weeks afterward.

Hendrix reports two cases of erysipelatous eruption from application of tincture of arnica. In one case the skin was everywhere œdematous, and the eruption covered the whole body and extremities. The entire abdomen was covered with a continuous blister, serum exuded freely from the whole abdominal surface, saturating cloth after cloth.

Paul Cagny states that the tincture of arnica has the same intensely irritating action upon the integument of the horse as in man. He reports a case in which arnica was applied to a bruise caused by the kick of another horse. The parts became hot, swollen, and excessively painful, and presented a blistered appearance. Such results, he observes, are of common occurrence from the use of this application in veterinary surgery.

The internal use of arnica is often followed by diaphoresis, erythema, and a sense of pricking and formication of the skin.

Phillips asserts that the irritating effects observed from arnica never follow the use of an aqueous solution, which contains none of the arnicine or volatile oil.

Piffard has suggested that the irritant properties of pre-

parations of arnica flowers may be due to the presence of an insect, the *Atherix maculatus*, and recommends that preparations made from the root should always be used.[1]

## ARSENICUM.

The cutaneous eruptions which follow the external and internal use of arsenic are similar in character.[2] While the external contact of arsenic produces certain changes in the skin which can in no way be distinguished from a dermatitis caused by other local irritants, the severer eruptive forms are probably due to absorption of the drug, and its specific action upon the skin. The irritant effect of the external application of arsenic was known to the writers of antiquity, and has since been studied by numerous observers.

If arsenious acid in a watery solution, or in the form of an ointment or paste, be applied to the healthy skin, there results inflammatory redness; and if the contact be continued sufficiently long, vesicles, pustules, &c., will form, attended with sensations of heat, burning, and pain, precisely as in the application of other vesicants. The hairs on the affected surfaces generally fall out, and there is exfoliation of the epidermis in large flakes. A higher degree of inflammatory disturbance is manifest in the production of erysipelatous swellings, sanguinolent eruptions, and ulcers, attended with toxic effects similar to those consequent upon the internal administration of the drug. Numerous cases are on record where arsenical lotions, plasters, and pastes have proved fatal. The application of an arsenical ointment (1 to 32) to a cancerous breast covering the space of one and a half inches, for one night only, caused death from poisoning on the second day. A strong application of arsenic is much safer than a weak one, since the intensity

[1] Piffard quotes Mercier ('Ann. de Cliniques,' 1811) as a recorder of symptoms of general irritation caused by ingestion of preparations of arnica flowers. Mercier referred these results to the contamination of the eggs and larvæ of insects in the flowers. Piffard never observed accidents with a tincture made from the root.—T. C. F.

[2] This statement is, we think, open to criticism, as will appear later on.—T. C. F.

of the inflammation it excites interferes with the action of the absorbents, and the effect remains local.

Abundant opportunities for the study of the changes in the skin caused by external contact have been afforded by the extensive use of arsenic in the form of lotions for the complexion, dusting powders, &c. A remarkable skin affection which prevailed among infants and children in Brighton in 1878, at first thought to be erysipelas, was traced to the use of a dusting powder containing 50 per cent. of white arsenic. Of twenty-nine attacked, thirteen died. The cases were carefully studied by W. H. Power, and the character of the eruption may be briefly described as follows :—In very mild cases there was erythema and the formation of minute vesicles ; in severer cases blisters and bladders formed in the creases of the skin where the powder was applied ; some of the bullæ when collapsed left black excavated sores, with indurated and discoloured edges. In fatal cases there was a generally blackened condition of the skin of the groins and pudenda, which quickly became somewhat swollen and hard. A like condition upon the abdomen was occasionally observed about and below the umbilicus, as also the skin of the axilla and folds of the neck. Invasion of these several parts where it occurred was simultaneous. In some instances vesication, variously described as "little white blisters," "yellowish bladders," or "bags of water," preceded or appeared about the same time as the blackness. The vesicles breaking discharged clear fluid, and left raw, black surfaces, which did not, it would seem from the description, take on suppurative or sloughing action. The average duration of the fatal illness was four or five days. The eruption was localised on parts of the body to which the powder was applied.

The various industrial uses of arsenic in the manufacture of artificial flowers, green-coloured cards, paper boxes, wall paper, and carpets, fixing dyes, &c., are the prolific source of numerous forms of eruptive disorders. Wood records a large number of cases of poisoning from arsenic contained in wall papers.[1]

[1] Carr points out that colour, even French white, whether in papers or other fabrics, or distempers, is no guarantee of freedom from arsenic. "The

It is well known that persons who wear *cheap* underclothing coloured with fuchsine, containing a large percentage of arsenic, or socks dyed with the same material, are subject to eczematous eruptions on the parts exposed to contact with the colouring matter.[1] Seifert reports the case of a lady who had been wearing stockings coloured with an aniline red containing arsenic. She was suddenly seized with all the symptoms of a gastro-enteritis and an

danger is simply in proportion to the quantity of arsenic contained in the colour, and to the facility with which it may be removed from the fabric either as dust or as gas," *i. e.* arseniuretted hydrogen. Workers engaged in mines, in the manufacture of arsenical compounds, or in the many industries in which the brilliant arsenical greens were formerly so much employed, are readily affected.—T. C. F.

[1] Erasmus Wilson, who drew special attention to the *dermatitis anilina*, wrote thus:—"Of a nature allied with arsenic, and according to some chemists as a consequence of the presence of arsenic itself, the aniline dyes have the property of exciting inflammation of the skin. Their effects have been observed both in the hands and in the feet, from the use of gloves and stockings coloured with those pigments. The feet, however, have been most frequently the victims, and the dyes in some instances have been transferred to the skin, while in others the pattern of the stocking has been found represented on the skin by tracings and figures of inflammatory hyperæmia. The dermatitis occasioned by the coal-tar pigments is frequently set up in the course of a few hours; it presents the characters of an aggravated eczema, and is attended with considerable effusion beneath the epidermis, which it raises up into large blebs, sometimes occupying the whole surface of the sole of the foot. . . . . Not unfrequently the inflammatory rash is transferred to the hands, even when those members have not been in contact with the poison, and a general irritation of the entire skin is sometimes set up by the process, which once was called sympathy, but is recognised now as propagated irritation. The progress of the dermatitis is always slow, and the inflammatory irritation liable to recurrences at intervals of a few weeks for a considerable period of time, sometimes for several months, and in a few instances for years."

Dresses, silk handkerchiefs, underclothing, chest protectors, hat linings, &c., have also been incriminated. The aniline dyes, brilliant or otherwise, of all colours, were largely used at one time for tincturing goods of all qualities. Arsenic, mercury, chromium, antimony, vanadium, &c., were often associated in the manufacture, and hence in any given case of dermatitis there is a difficulty in determining without analysis to what extent the irritation is due to the aniline dye or some other agent. A great number of cases of *aniline dermatitis* might be collected in addition to those here referred to.

Wilson mentions a severe dermatitis excited in workmen by contact with an acid volatile "aniline orange dye."—T. C. F.

acute hæmorrhagic nephritis, besides an eczematous eruption on the dorsal surfaces of both feet. The urine for some time afterward contained a small amount of albumen. Impetiginous eczema has been seen on the arms of a lady who wore a bracelet composed of a paste containing a large proportion of arsenite of copper. According to Rollet, who has made a careful study of the cutaneous lesions from the industrial uses of arsenic, erythema is the first degree of arsenical dermatitis. Generally upon the erythema are developed other elementary lesions; papules which enlarge and extend, and are covered with small scales of greenish tint, fine, transparent vesicles, and, finally, pustules. These pustules form with conical projections, red at the base, purulent at the summit, and are covered with a small, opaque, yellowish-green crust. If the irritation continues, the pustules become the points of departure of ulcerations, which progressively increase in breadth and depth. Arsenical eruptions are situated upon parts exposed to contact with the irritating cause, as the face, forearms, hands, interdigital spaces, also the feet and inguino-scrotal region. The genital parts are peculiarly susceptible to the irritant action of arsenic. Frequently there are large ulcerations with œdema of the scrotum.[1]

[1] Guy described the eruptions as appearing under many forms; as a diffuse erythema, as small and crowded vesicles, as papules which grow flatter and wider by contact with an opposed portion of skin, and lastly, as pustules running into ulceration and gangrene. He commends the portraits given by Vernois. The ulcers on the scrotum, he adds, are peculiar and highly characteristic, *i. e.* small shallow ulcers, with even surface and thin soft edge, barely moistened with a light yellow discharge, perfectly circular, as if cut out by a sharp round punch, penetrating through the skin, and no further. It is such ulcers as these which, forming on the face and other parts of the body, leave the circular scars so similar to those of smallpox.

The arsenical powder diffused through the air, and conveyed by the fingers, inflames the mucous passages by which it enters, and the skin, especially of the face, neck, the large flexures, the pudenda, &c. The ulcers on the green-stained hands in those who handle the products are very characteristic. These changes are evidently solely due to direct contact with the arsenical compound, but as poisoning progresses the local effects probably become intensified, and other eruptions may arise.

Butlin discusses the alleged liability of tin and copper smelters to cancer of the scrotum from the effects of arsenious acid, and concludes that these workers have no such special liability.—T. C. F.

I observed several years ago at the New York Dispensary an eczematous eruption, with deep-seated pustules, on the hands of two young women who were employed in a paper box manufactory, in which variously coloured glazed papers were used.

White reports several cases of arsenical dermatitis, one of intertrigo in an infant, the brown spots resembling pityriasis maculata et circinata of the mother, which were probably due to absorption of arsenical pigments contained in the wall paper, as every other possible factor was eliminated—a theory sustained by the fact that there was immediate improvement upon removal of the patients from the room. Clarke records eczematous eruptions and nasal ulcerations as due to the emanations from arsenical wall papers.

Allen reports having observed several cases of arsenical dermatitis, especially marked on the hands, legs, and feet, in longshoremen engaged in unloading a cargo of dry hides which had been cured with arsenic. The arsenical dust had sifted through their clothing and low shoes, producing large vesicles and bullæ, followed by ulceration with swelling of the feet, legs, and hands. Papular and erythematous patches, attended with burning and itching, were scattered over the legs and thighs.[1]

Perhaps no drug in the materia medica exerts a more marked influence upon the nutrition of the skin than arsenic. Almost all observers have noted its tendency to aggravate eczematous and other acute inflammatory disorders of the skin. Devergie was the first to signalise the fact that cutaneous lesions may be caused by the internal use of arsenic. A most complete and careful study of the arsenical eruptions has been made by Imbert Gourbeyre, and embodied in his admirable monograph upon this subject. According to this authority, the pathogenetic influence of arsenic may be manifested in the form of papular, petechial, urticarial,

[1] Steel has called attention to the occurrence of a pustular rash from sheep-washing. Cooper Forster described a painful inflammation of the finger ends and nails, which was exceedingly common years ago among the students, when the use of arsenic was first introduced to preserve subjects for the dissecting room.—T. C. F.

vesicular, erysipelatous, and pustular eruptions.[1] To these may be added an erythematous or scarlatiniform eruption, the occurrence of which has been attested by numerous observers.[1]

The various preparations of arsenic differ in no sensible degree in their effects upon the skin, so that observations relating to arsenious acid will apply to Fowler's solution, the arsenite of soda, Asiatic pills, &c.

*The erythematous form.*—Although an erythema is the commencing stage of several of the forms of arsenical eruption, it rarely represents the acme or completion of the inflammatory process. Martens Pereira observed in a gouty patient, after taking one sixth grain of arsenious acid a day, on the third day an intensely red eruption on the face, neck, upper part of the body, and flexor surfaces of the joints, with œdema of the eyelids.[2] The eruption disap-

[1] Erasmus Wilson states that besides occasioning erythematous dermatitis, inflammation of certain mucous membranes, such as the conjunctiva, nose (leading to ulceration and perforation of the septum), and pulmonary passages, the internal administration of arsenic may produce discoloration from excessive pigmentation and desquamation, and on the palm of the hands and sole of the feet not only desquamation, but also thickening of the epidermis to a considerable degree from hypernutrition, and may occasion the formation of minute granular corns, each little corn corresponding with the aperture of a sudoriferous duct. Jonathan Hutchinson maintains also that the prolonged use of arsenic may seriously depress the nutrition of the skin, and set up local neuritis, leading to the formation of scaly patches like psoriasis, most obvious on the elbows and backs of the knuckles, and to warty or corn-like indurations (keratoses, arsenic corns), which may acquire a tendency to pass into epithelioma. The skin generally may assume a dry, harsh, muddy, or hyperpigmented appearance. The corns tend to form mostly on the dry palms and soles. Hutchinson suspects that certain opacities in the vitreous humour own a similar causation. Reboul cites cases in which the palms and soles were the seat of a desquamating erythema. Hunt says that "in the exceptional cases tenderness of the soles of the feet, and more rarely of the hands, present the first indications of a full dose. The tenderness is sometimes succeeded by a thickening of the epidermis, which subsides ultimately." James Stewart noted a recurrence of wart-like excrescences on the *dorsal* surface of the fingers and hands, which quickly disappeared when the arsenic was stopped. McCall Anderson says "an erythematous rash, too, is not uncommon, especially on the face, neck, palms, and soles, and in the last situation this may be followed by great thickening and induration, which has a papulated character." See Pringle, Crocker, and Brooke on arsenical keratosis and hyperidrosis of the palms and soles.—T. C. F.

[2] Hunt laid great stress on the conjunctivitis which "in about forty-nine

peared between the third and fifth days, but desquamation n large flakes continued for nearly two months.

Macnab has observed a rubeola-like exanthem in patients vho had taken small doses of arsenic, three-drop doses of Fowler's solution, daily for three weeks.

Hyde saw in a young woman, who had taken only three nedicinal doses of Fowler's solution, a light red scarlatini-form blush, with a few isolated vesicles, covering both shoulders, the eruption being present, but less distinct, on the hands and face. Piffard gives numerous references of erythematous and rubeoloid eruptions consecutive to the internal administration of arsenic.

*The papular form.*—According to Imbert Gourbeyre, the papular form occurs as discrete, pin-head sized papules, first in scattered groups, which unite later to form lenticular papules, occasionally large disseminated patches, which sometimes resemble a papulo-syphiloderm, although of a less coppery hue. The parts affected by preference are the face, neck, hands, and genital organs. The eruption usually disappears in five or six days, followed by furfuraceous desquamation. In one case the papules increased in numbers until they gave the skin the appearance of "goose-flesh." The eruption was attended by decided itching, and lasted some days after the discontinuance of the medicine. Stewart reports the case of a powerfully built man, who was ordered five-minim doses of Fowler's solution after each meal. After the sixth dose he felt feverish, and he noticed that his hands and arms were red, swollen, and very hot; the redness of the skin spread rapidly, until it involved the entire surface except the face. The skin was covered with countless papules, about the size of millet seeds.[1]

cases out of fifty takes precedence of the more grave affections which indicate an over-dose." Observers have recorded considerable œdema of the eyelids and face, which has been described as "erysipelatous dermatitis." Crocker and McCall Anderson mention puffiness or plumpness of the hands and face.—T. C. F.

[1] Devergie says an eruption may appear consisting of red, isolated, papular boutons, of the size of a lentil, which slowly multiply and increase if the treatment is continued. Hunt stated that "now and then a delicate papular eruption (lichen arsenicalis) will show itself suddenly under a course

Keys, cited by Piffard, reports after the use of arsenic, doses not stated, a papulo-erythematous eruption, dry and livid, on wrists and neck; general papular eruption on trunk and extremities, attended with pruritus. Baglie observed dryness of the skin, heat, and itchiness of the eyelids, with the production of a minute papular rash, followed by desquamation. Faithful observed a papulous eruption about the face, attended with a decided amount of pruritus. The papules varied in size from a pin-point to that of a No. 4 shot; they were discrete, and more or less scaly upon their summits. The eruption disappeared after a few days upon the discontinuance of the drug, followed by furfuraceous desquamation of the parts affected.

*The urticarial form.*—Fowler, whose name is so well known in connection with this drug, in his medical reports on the effects of arsenic, was the first to instance urticaria as one of the results of its employment. According to Imbert Gourbeyre, it is one of the most frequent forms of arsenical eruption. The wheals are white or rosy-red, and extremely pruriginous, differing in no essential particular from urticaria as commonly observed. Berenguier reports the case of a young lady treated with arseniate of iron, which brought out a copious eruption of white, somewhat reddish elevations of the uniform size of a lentil, and accompanied by intense itching. Broadnax states that arsenic produced a rubeolous eruption in two per cent. of one hundred and ninety-seven cases in which it was administered.

*The vesicular form.*—The occurrence of a vesicular eruption from the ingestion of arsenic has been recorded by numerous observers. This eruption may sometimes assume an eczematous character which, according to Balfour, may prove extremely obstinate. Ringer says eczema or urticaria may arise, or perhaps vesication or mere desquamation with tenderness of the hands and feet; again he says, in arsenical poisoning, a petechial papulo-vesicular or wheal-like rash often appears from the second to fifth day.

Finlayson saw an eruption of clusters of vesicles on an inflamed base, extending from lower part of the arm down

of arsenic, and as suddenly disappear under a few doses of the Liq. Ammon. Acet."—T. C. F.

back of the forearm and hand, including backs of the ers. Herpes labialis and preputialis, and an eruption of pes upon the scrotum, have also been observed from the of arsenic. Faithful states that in one case herpes pre- ialis always made its appearance after giving arsenic for ew days.

It has been asserted that herpes zoster may occur as the ult of the ingestion of arsenic in medicinal doses. Hutch- on, while not claiming that a causal connection has been olutely demonstrated, yet suggests its extreme probability view of the well-known fact that herpes zoster has been re often observed in patients who have been taking enic than in those not subjected to this medication. He orts a number of cases, fifteen or sixteen, in which the ncidence was so marked as to furnish strong presumptive dence of an etiological relationship. His observations ve been supplemented by the experience of many other rmatologists who have noted this coincidence.[1]

*The pustular and ulcerative forms.*—According to Imbert urbeyre, the internal use of arsenic may produce a pustular ıption resembling variola, the lesions terminating in crusts ulcerations leaving cicatrices.

Orfila has noted, as one of the toxic effects of the drug on e cutaneous system, an eruption of pustules on the face, oulders, arms, and chest.

Bazin reports a case in which there appeared after minute ses of arseniate of sodium, continued for fourteen days— e half of a grain altogether—an eruption of discrete pus- les in various stages of development, limited to the hypo- strium and right flank. One of the pustular lesions had

[1] This observation has now become the common property of the majority dermatologists, though many still hold that the occurrence is a mere ıcidence. Our increased knowledge of the production of peripheral ıritis by arsenic furnishes a ready explanation, though it may be noted t in many cases of arsenical peripheral neuritis zoster is not developed. e occurrence of zoster in carbon dioxide poisoning is an analogous fact. ilsen examined the statistics of psoriasis cases in the Copenhagen Hospital, l found that zoster occurred in 7·8 per cent. of those to whom arsenic was ven, whilst no eruption of zoster was found in those who received no enic. The latter class was, however, more than a third less numerous ın the former.—T. C. F.

become transformed into an ulcer, a centimetre in diameter, surrounded by indurated and inflamed tissue. Near by were two large ecthymatous pustules just breaking down in the centres into ulcers; other lesions were passing from a papular into a pustular form. The evolution of the lesion through its various stages, from appearance of papule to cicatrisation of ulcer, occupied only a few days. The patient rapidly recovered as soon as the arsenic was stopped. In this case as in others, pustular lesions are the points of departure of the ulcerations encountered in various parts of the body, more especially on the head, limbs, and scrotum. Gangrene sometimes occurs around the genitalia.

Erysipelas with bullæ, erysipelatous inflammations about the face and eyelids, and eruptions of a petechial character, affecting by preference the trunk and genital parts, have been recorded by Bazin, Imbert Gourbeyre, and others.

According to Morris, boils[1] and carbuncles occasionally result during a course of arsenical treatment. This statement is confirmed by Foster, Vaudry, and others cited by Piffard.

*Brownish pigmentations.*—Among the incidental effects of arsenic upon the skin may be mentioned certain greyish or brownish discolorations, which are especially liable to occur upon the face and various parts of the body after its prolonged use. Wilson reports the case of a patient with gutta rosacea, who had taken arsenic for two months, when there was noticed a change in the colour of the skin, first over the abdomen, then on the neck, breast, face, and hands. The face was of a yellowish-brown colour, the eye ball dark, the skin of the entire body more or less pigmented; chronic erythema affected the palms; there were hard dry points at the orifices of the sweat-glands; the eyelids and the extremities were œdematous. In a case of arsenical dermatitis recently presented by me before the New York Dermatological Society, there was an erythemato-papular eruption

[1] Reboul cites two cases, and H. C. Wood records the case of a man who ate a preparation called "Rough on Rats," and suffered from gastro-enteritis, and in some days swelling of the face, then of the body, and from a red rash with small watery blisters, a general outbreak of boils, and multiple neuritis.—T. C. F.

with a greyish-brown, almost black discoloration of the surface, especially marked over the abdomen and inner surface of the thighs. Guaita reports that, in fourteen children placed upon Fowler's solution for four or five months, there was observed a bronzed appearance similar to that of Addison's disease, beginning on the neck, extending to the chest, then to the abdomen and hands; at times it is seen on the back and legs. It disappears by desquamation in about four weeks. Bazin has characterised this pigmentation as a tint comparable to the staining of nitrate of silver. This condition depends, according to Gubler, not upon a chemical combination, as is the case in argyria, but on abnormal pigmentation.[1] Wyss saw alopecia areata developed by the prolonged internal use of arsenic. This result

[1] Devergie called attention to the fact that when a scaly disease is undergoing cure under the influence of continued arsenical treatment, the healed patches assume a brown colour. He called these patches "taches arsenicales," and considered them an indication of the perfect cure of the patches of disease. According to his observation they only disappear after eight or ten months. Thomas Hunt, on the other hand, claimed priority for the observation that a secondary effect of continued arsenical treatment was to cause a wide-spread pigmentation. "The trunk of the patient first, and subsequently all those parts of the body which are by the dress protected from the access of light and air, become covered with a dirt-brown, dingy, unwashed appearance, which under a lens reveals a delicate desquamation of the epidermis, and is, in fact, a faint form of pityriasis." He stated that this effect was so common among persons of fair complexion or delicate skin, that he was not sure it was not the rule rather than the exception. It quickly disappeared in a very few weeks after the arsenic was discontinued.

The occurrence of this diffuse pigmentation, the *melasma arsenicale* of Wilson, the *arsenmelanose* of Wyss, with desquamation has now long been a well-established fact, and the appearance is familiar to those who have occasion to carry out a continued arsenical treatment. Several observers mention the occurrence of a less intense pigmentation on exposed sites, such as the face and hands.

Wyss made sections of the skin in two cases of diffuse pigmentation. He found that the pigment in recent and slight cases is deposited as little grains in the lymphatic spaces of the papillæ, and to a less extent in the derma. In inveterate and intense cases the pigment is in far greater quantity in the lymphatic area of the dermis. It is to be found also in the rete. Congestion of pre-existing areas of eruption is frequently seen during arsenical treatment, and I agree with Hyde that erythism of the healthy skin is not uncommon, though often unnoticed, and I believe that the pigmentation and desquamation is a sequence of such constantly recurring hyperæmia.—T. C. F.

he thought due to the effect of the drug upon the trophic nerves of the hair-follicles, causing disturbance of nutrition.

As regards the pathogenesis of arsenical eruptions opinions differ. It is known that arsenic is eliminated, not only by the kidneys, but by the glands of the skin, the mucous membranes, the salivary and lachrymal glands, &c. Chatin found arsenic in the contents of a bulla, and Bergeron and Lemattre in the sweat of patients undergoing arsenical treatment;[1] while Barella claims to have demonstrated the direct elimination of arsenic by the sweat-glands. Therapeutically arsenic has been classed as a neuro-tonic, and is supposed to modify cell nutrition through its influence upon the peripheral nervous plexuses. In view of these facts we can understand how it may cause disorders of the capillary circulation and disturbances of the nutrition of the skin, as manifested in the various forms of eruptive disorder above described.

The tests for the detection of arsenic are so elaborately considered in text-books that it is unnecessary to describe them in detail. The reader is referred, for information upon this point, to page 419.

The treatment of arsenical eruptions may be restricted to the simple expedient of suppressing the offending cause. In the more severe forms the same local measures are to be resorted to as are indicated in dermatitis from other causes.

### BALSAMUM PERUVIANUM.

An erythematous and also an eczematous eruption are by no means infrequent from the irritant action of this agent.

Mögling, quoted by Lewin, reports an urticarial eruption following a single application of the balsam of Peru for the cure of scabies in his own person. Redness of the skin in

[1] Reboul failed to detect arsenic in the sweat and scales of a psoriasis patient, who on the fifteenth day of treatment was taking sixty drops of Fowler's solution daily.—T. C. F.

### AVA.

Numerous references will be found in books of travel and works on the diseases of Polynesia to the influence of the *Macropiper methysticum* (the ava or kava of the South Sea Islands) in producing a severe scaly disease of the skin.—T. C. F.

patches appeared on the inner surfaces of the knees and on the shoulders, attended with intense itching. The wheals first appeared on the abdomen, arms, and shoulders. The urticaria successively affected the face, neck, back of forearms, legs, and dorsum of the feet. It disappeared when he removed the woollen shirt he had worn, and which was saturated with the balsam, and had taken a warm bath.

### BELLADONNA—ATROPIA.

The exanthem produced by the external or internal use of belladonna, or its alkaloid, is usually erythematous in character. It consists of a bright diffuse redness, strikingly suggestive of the rash of scarlatina.[1] It is usually confined to the face and neck, but may extend to the upper portion of the chest, and, exceptionally, may become generalised over the surface. It is quite fugitive, disappearing in the course of a few hours, leaving no trace, and is not, as a rule, followed by desquamation.

The belladonna rash is most commonly and characteristically seen in children with fine, delicate skins, in whom it appears after small doses of the drug. Its evanescent character is a marked feature.

Lusanna reports a case in which, after a small dose of atropia, the skin became intensely red, and presented the appearance of having been exposed to the intense heat of the sun. The erythema lasted from one half to one hour, and came out each time after taking the drug. Stadler saw a similar eruption appear upon a child within a few minutes after the administration of one two-hundredth grain of sulphate of atropia, which lasted five hours. Smaller doses

[1] Diffuse or patchy flushing of the face and neck and trunk, sometimes with swelling, and a pungent heat of the surface generally, are common incidents of belladonna poisoning. The wide-spread, punctate, scarlatiniform eruption, "la scarlatine belladonnée," is of rarer occurrence.

The local eruption excited by the external application of belladonna (emplastrum, linimentum, glycerinum, &c.) frequently becomes vesicular or pustular, and then has been described as herpetic. It may extend considerably beyond the site of application of a plaster, or the more or less generalised scarlatiniform rash may ensue. The belladonna rash is referred to in many works on diseases of the skin, therapeutics, medicine, and toxicology.—T. C. F.

brought out the eruption each time, but it was of shorter duration. In a case reported by Gray, the face, the upper extremities, and trunk exhibited a diffuse scarlet efflorescence studded with innumerable papillæ resembling very closely the rash of scarlatina. A patient of Dreyfous took two grains of extract of belladonna in three days, followed by a vapour-bath. On the night following the third day there suddenly appeared a scarlatiniform eruption mingled with lesions like those of papular erythema, and in places with vesicles. The eruption, which was attended with intense pruritus, occupied almost the entire surface of the body, disappearing on the fourth day without desquamation. Boecke reports a case in which one quarter grain of extract of belladonna, ordered three times a day to a consumptive patient, produced, after the second dose, erythema and partial gangrene of the skin of the scrotum.

In a case which came under my observation, a child four years of age was given an aperient pill containing one quarter grain of extract of belladonna, which had been ordered for his father. In the course of an hour or two there was an excessive flushing of the face, which soon extended over the body. When I saw him, two hours later, the whole surface of the body presented a "boiled lobster" appearance; there was redness of the eyes and throat, and mydriasis. The next day the erythema had disappeared, leaving no trace.

Köbner observed a characteristic hyperæmia of the face from the use of suppositories containing extract of belladonna introduced *per vaginam*.

Wilson reports the cases of two lying-in women who applied belladonna to the breasts to produce galactostasia. On the fourth day a scarlatina-like exanthem came out, which disappeared in the course of three or four days without desquamation.[1]

Mackintosh reports a case of herpes following the external use of belladonna and atropine. The application of belladonna liniment to an inflamed knee-joint was followed

[1] Dr. Herbert Spencer and others have informed me that such a rash will occur on rare occasions after the application of belladonna applications over the breasts or abdomen.—T. C. F.

by an eruption of herpes with a good deal of swelling over the seat of application. Two months later he was ordered a solution of atropine for iritis; some of the solution ran over the cheek, and was in a few hours followed by an herpetic eruption of exactly the same character as had followed the use of the belladonna liniment.[1]

It is a clinical fact familiar to ophthalmologists, that the use of atropine drops, instilled into the eyes, occasionally causes an erysipelatous inflammation about the lids and face, sometimes giving rise to considerable disfigurement. Chislom has recorded a case of severe facial erysipelas from the topical use of atropia.

Liebreich has noted that conjunctivitis, erythema, eczema, and peculiar pearly granulations on the conjunctiva are observed after the long-continued use of a solution of atropia instilled into the eyes.[2]

Fialkowski reports a case in which a solution of atropine instilled into the eyes produced on the second day an erythema and eczema of the eyelids. The atropine being continued for ten days, almost the entire face of the patient presented a general confluent eczema. The solution being discontinued, the eczema disappeared in the course of ten days. A new instillation of a single drop of a weak solution caused the appearance of vesicles, with pruritus of the borders of the lids.

The belladonna rash derives its chief clinical importance

[1] Cæsar records a case in which blistering followed the use of a belladonna plaster, extending just beyond the site of application. Some time later a plaster was again applied, and caused a vesicular eruption on a red base occupying the whole left side of the trunk, and bounded by the iliac crest and the mid-lines before and behind. Later again it was shown on two occasions that fifteen drops of Tinct. Bellad. given thrice daily brought out a scarlatinal rash on face, chest, and arms, with the usual dryness of the throat, &c.—T. C. F.

[2] Brudenell Carter has written that when atropine has been long in use, even the purest and most neutral solution is apt to cause local irritation in some persons, and this irritation is usually more manifest in the eyelids, and especially on the lower lid and on the adjacent skin of the cheek, than elsewhere. It may be readily recognised by a peculiar dryness and stiffness of the inflamed skin. The severe erysipelas-like acute inflammation seen in certain persons with a special idiosyncrasy is rare, although but few ophthalmologists have failed to meet with such cases.—T. C. F.

from the fact that it sometimes simulates scarlatina with alarming accuracy, especially when associated with congestive symptoms of the throat and fauces. The bright scarlet hue of the eruption renders this similitude quite complete, although the punctate character of the scarlatina rash is usually not present. The absence of fever and other prodromal symptoms, the dilatation of the pupils, and the transitory existence of the belladonna exanthem soon clear up the diagnosis.[1]

The mode of production of the belladonna eruption has been attributed either to a direct excitation of the sympathetic or to a paralysing influence of the drug upon the vaso-motor centres, causing dilatation of the cutaneous capillaries. The exceedingly evanescent character of the eruption renders special treatment unnecessary.

### BENZOLE.

Lewin has observed that the application of benzole as a parasiticide on the inner surfaces of the thighs and scrotum, and on other sensitive surfaces, causes intense pain, lasting several minutes, which is followed by more or less extensive erythema.

### BROMINE—BROMIDES OF POTASSIUM, AMMONIUM, SODIUM, LITHIUM, ETC.

The cutaneous disturbances which may follow the ingestion of the bromine compounds have been long recognised by the profession. All of the salts above enumerated produce similar effects upon the skin. The eruptions recorded as due to the use of bromide of potassium may be regarded as typical of those produced by the other bromine preparations.

The so-called "bromic acne" occurs in so large a proportion of persons who take the bromides that it is difficult

[1] It is well known that children tolerate belladonna to a remarkable degree. The rash is certainly rare, when it is remembered in what large doses belladonna is frequently administered. Dreyfous says the rash, which is scarlatiniform at the outset, may later on approach the eczematous or erythema papulatum type.—T. C. F.

to separate these irritative effects upon the skin from the recognised physiological effects of the drug. This proportion is given by Clark and Amory as sixty-six per cent., and by Voisin as seventy-five per cent. of all patients treated with bromide of potassium. The latter observer records the fact that, of twenty-four epileptics successively treated, all were affected by bromic acne on the face, scalp, back, and other parts of the body.

The term "bromic acne," it may be remarked, is quite comprehensive in its signification, and has been used to designate a variety of anatomical forms, some of which are in no way connected with disorders of the sebaceous glands.[1]

The bromic eruptions have been most carefully studied by Voisin and Veiel. The classification of the former, which embraced all changes in the skin which had at that time been recognised as due to the administration of the bromides, has been enlarged by the addition of other varieties of eruptive disorder which have since come under observation.

*The erythematous form.*—Veiel describes a diffuse erythema, always limited to the lower extremities, accompanied by high fever, and quite painful. According to other observers, it may occur as a bright red or dusky red rash, in patches the size of a finger-nail or a pea, and not absolutely confined to the lower extremities. Bedford-Brown has noticed the occurrence of a roseola from bromide of potassium in children. Comparatively few observations of this nature have been recorded, probably because this drug is seldom administered to children, and not because they are insusceptible to its pathogenetic effects. Carlos reports a

[1] The bromic eruptions have a remarkably close resemblance to those produced by iodine preparations, but the experienced eye can generally separate them by delicate characteristics which it is difficult to portray in words. The essential lesion in both is a dermatitis with a special localisation about the sebaceous apparatus. The primary lesions in both may take the form of maculo-papules, papules, papulo-vesicles, papulo-pustules, tubercles, tuberculo-pustules, tubers, vesicles, and bullæ. There is a tendency to the formation of conglomerate lesions by confluence. We can also observe secondary crusting, papillomatous overgrowth, and ulceration. Bromic eruptions, however, tend to be more indolent and tardy, and acute bullous lesions are rarely observed.—T. C. F.

case in the service of M. Voisin in which bromide of ammonium produced an eruption of slightly elevated patches of a vivid red colour, with subcutaneous induration. The eruption first appeared on the thighs and abdomen, and became general. It disappeared with considerable desquamation.

*The urticarial form.*—Voisin observed in two cases, out of ninety-six upon which his studies were based, an eruption, preceded by pain and pruritis, of oblong or irregularly rounded elevations of the skin of varying size, from one fifth to two and a half inches in diameter, and of a rose-red or cherry colour. They presented the shape, colour, and hard base of erythema nodosum, but resembled urticaria in reappearing when rubbed.[1] These lesions persisted so long as the bromide was given, but they rapidly disappeared on the discontinuance of the drug, always leaving behind the subcutaneous nodosities which were slower in evolution. Veiel also observed coin-shaped, wheal-like elevations, varying in size from one quarter to one half inch in diameter, develop on erythematous patches of skin, but only upon the legs. They were very sensitive to the touch, and if the drug was continued they took on a suppurative action. Richard, cited by Deschamps, reports the occurrence of an eruption developed upon erythematous patches, and presenting the objective character of an urticaria, in a boy six yearsold, from large doses of bromide of potassium. The eruption was distributed over almost the entire surface of the body.

*The papular form.*—The papular bromide rash is most often observed as the first stage of bromic acne, to be succeeded by a papulo-tubercular and pustular stage. Duhring describes a case of maculo-papular eruption, in which small doses of the bromide produced an erythematous condition of the skin of the face and neck, accompanied by a copious eruption of maculo-papules and flat papules. The dark coppery colour of the eruption simulated very closely a maculo-papular syphiloderm. Echeverria describes a papular

[1] Inflammatory nodules involving the skin to a considerable depth, and closely simulating erythema nodosum in appearance, have been frequently observed. These nodes may become covered later on with little pustular points and finally a dark crust, and they may fungate or ulcerate.—T. C. F.

eruption distributed over the elbows and surfaces of the hands, knees, and legs.

*The papulo-pustular form, "bromic acne."*[1]—This is by far the most common and characteristic form of bromine eruption. Bromic acne exhibits in the manner of its development, its seat of election, and the anatomical form of its constituent elements many points of similarity, if not of identity, with acne vulgaris. As in acne vulgaris, we find associated papules, tubercles, and pustules affecting by preference regions rich in sebaceous glands, such as the face, back of shoulders, front of chest, &c.; but, unlike ordinary acne, they often surpass these habitual limits, and they always develop without the antecedent existence of comedones. Bromic acne manifests a special preference for parts where hairs abound; it attacks the hairy scalp, eyebrows, hairy portions of thighs and legs, and many of the pustules are found pierced with a hair. It is not limited to the young, as acne vulgaris. Sex, age, disorders of the reproductive organs, &c., do not act as predisposing causes.

The papular form usually precedes the pustular form. It is most commonly seen on the hairy scalp, about the forehead and nose and back of shoulders, rarely on other parts, in persons who have thick, greasy skins, or a free secretion of sebaceous matter. They commence as pin-head or pea sized hyperæmic patches developed from an indurated base, and surrounded by areola; the majority of the papulo-tubercles are pierced by a hair. They may remain in this condition for weeks, indolent and without tendency to undergo progressive change, or they may rapidly develop into the pustular form.

The pustules are of a yellowish-white colour, similar to those of acne vulgaris, and may sometimes present an ecthymatous aspect. Sooner or later the contents of the pustules are discharged, and a firm indurated nodule or a pigmented spot remains. After healing, they not infrequently leave small depressed, rounded cicatrices. The pustular condition may persist almost indefinitely if the use

[1] The eruption here described is that usually seen in adults. The phase occurring in infants is that described further on under the term "confluent acne."—T. C. F.

of the drug be continued. Veiel found that the number and development of the pustules increased with the augmentation of the dose. Exceptionally, it has been observed that the eruptive accidents, after having persisted for some months, rapidly disappear and are not again reproduced, although the medicine may be continued in the same or augmented doses. Ordinarily, the eruption disappears in the course of one to three weeks after suspension of the drug.

Voisin describes an eruption of small tumours formed by groups of indolent acneiform pustules, inflamed at the base and depressed at the centre, very painful to the touch, except at the centre, which is anæsthetic. They discharge a matter like that of furuncles, and are sometimes transformed into foul atonic ulcers, which heal slowly and leave cicatrices.[1] They are usually seated upon the legs, and may coexist with acne over other parts of the body.

*Confluent acne.*—Under the designation of "confluent acne," Cholmely has described an eruption occurring in a boy thirteen years old who had taken twenty-five grains of the bromide three times a day for a week. The eruption was at first varicelliform, but the vesicles, instead of drying up, became in many places confluent, the clusters so formed continuing to enlarge and showing numerous points of suppuration. The eruption, though occurring on other parts of the body, was most active on the legs. The lesions were of various sizes, from a pea to a fourpenny piece, larger than those on the face, irregularly oblong. The most recently formed consisted of a prominent circular vesicle, filled with milky-white semi-fluid matter, seated on a slightly elevated and hardened base, and surrounded by a vividly red areola, pierced by one or more broken hairs. The larger spots were flattened elevations, covered by a flaccid cuticle or thick light brown crusts, and surrounded by a dark red areola. On removal of the crust, the surface beneath presented numerous millet-seed-like, yellowish protuberances. The eruption died away after seven weeks' duration. The bromide, in full doses, redeveloped the eruption on the sixth day.[2]

[1] Beneath the crusts papillary hypertrophy may occur.—T. C. F.

[2] The eruption described by Cholmely is the type of that usually met

Neumann states that he has observed an eruption very much like molluscoid acne coming out in successive outbreaks, and in another case a carbuncular eruption, consisting of infiltrated tumours, with considerable loss of substance in the centre.

*The furuncular and anthracoid forms.*—A furunculoid eruption has been observed by Voisin and many others.

Smith and Neumann saw numerous boils on different parts of the body from the use of the bromides; the latter observed them on the hairy portions of the face and on the forehead and neck. These boils were for the most part of small size, and without central core. It is doubtful whether they differed in their anatomical seat from ordinary boils.

Quite recently I have observed an eruption from the prolonged use of bromide of potassium which cannot be grouped with any of the preceding forms.

In June, 1886, a patient who had been taking a mixture of bromide of potassium and tincture of iron almost continuously for several months presented himself, with a large carbuncular swelling upon the right arm at the insertion of deltoid. He stated that three days before it appeared as a "large reddish pimple," which within twenty-four hours developed into a blister. This broke the following day, showing four or five openings from which pus exuded.

Within the next two weeks similar lesions developed upon other portions of the body. One appeared upon the

with in infants. The earliest lesions consist of miliary follicular papules, which become capped with fluid, either opaque or puriform in character. Here and there vesicles are seen with comparatively little solid base, and varicelliform in appearance. More rarely vesicles and even bullæ may be seen rising directly from the skin, apparently without a precedent solid stage. There is a marked tendency for the lesion to evolve in groups, and thus larger patches are formed, often seen to be studded with minute puriform heads. These patches may extend by a vesico-pustular margin, become covered with dark crusts, and raised up by an increase of inflammatory exudation. There is a tendency to papillary hypertrophy, so that many lesions may closely simulate condylomata. I have a drawing of a case in which large formidable-looking tumours existed on the legs of an infant.

This so-called "confluent acne" is sometimes seen in the adult. The peculiar brownish-red, encrusted, papillated patches on the legs are very characteristic.—T. C. F.

left wrist, two on inner side of left thigh, two on right leg, one on left cheek, and another on the back of the right shoulder near posterior axillary space. I had an opportunity of watching the mode of their formation and evolution, which was as follows:—First there appeared a circumscribed inflammatory swelling, which in twenty-four hours was surmounted by a flat bulla, filled with a sero-purulent fluid. The swelling rapidly increased in depth and extent, resulting in the production of a hard phlegmon, surrounded by an intense inflammatory areola two or three inches in diameter. Upon rupturing the blister there was disclosed a number of openings, from which a rather thin pus could be pressed out. On probing, the openings were found to be shallow. The lesions differed from ordinary anthrax in their more indolent and superficial character, the comparative absence of pain, and the rapidity of their involution. After the bromide was discontinued, they disappeared within a few days under the influence of dressings of camphorated oil.

*The ulcerative form.*—Seguin has narrated three cases in which a peculiar cutaneous lesion, termed by him *ulcus elevatum*, was produced by bromide of potassium. The lesions were described as large, irregular ulcerated patches, raised from two to four millimetres above the surface, symmetrically situated on legs. The elevated floor of the ulcer was firm, greyish red in colour, with here and there an adherent crust. It secreted a sanious, fœtid, puriform liquid, and bled upon being touched. It did not look like ordinary granulating tissue; it was much firmer, and composed of large masses. At several points it presented a slightly villous, or rather papillomatous appearance. The cicatrix of a similar lesion, which had existed ten years ago, was seen. The patient at that time had been taking large doses of the bromide. In the third case the lesion had been twice developed by bromides, but it was more carbuncular in character.

Amidon describes what he terms an "epithelial ulcer," peculiar to the prolonged use of the bromides in large doses, of which he had observed two or three cases. It begins as a large-sized, single acne spot, with a large base, which

apparently takes on an inflammatory process, and afterwards breaks down into what appears to be a simple ulceration. Vesicles appear in circular form about the ulcer, the contents of which become cloudy and purulent, and are finally covered with dark-coloured crusts. The centre of the affected surface heals, while a superficial ulcerative process extends at the periphery sometimes to the distance of several centimetres. The true skin is not involved; the process simply denudes the skin of its cuticle, with hypertrophic changes affecting the papillæ.

Sangster reports a bromide eruption presenting the following characteristics:—On the outside of the right leg there was a round, considerably raised patch, about the size of half a crown. The surface was partly crusted; here and there it exhibited little subcutaneous dots of pus closely set together. There was a crop of smaller blotches over the same thigh and buttock, the size of a threepenny piece, elevated and partly covered with a brownish crust. Two symmetrical groups of similar lesions, four in number, on either side of the face, completed the eruption.

*The verrucose form.*—Veiel records an anomalous form of bromine eruption in which he observed large wart-like prominences upon the face, cheeks, nose, and eyebrows of a boy sixteen years of age, soon after he commenced taking the bromides. These lesions exactly resembled the verruca ordinarily seen upon the hands of young persons. This phenomenon has not been encountered, or at least recorded, by other observers, and it may have been a coincidence, rather than an effect directly due to the drug.

*The vesicular form.*—In Voisin's classification of the various forms of bromine eruption, he reports a case coming under his observation of moist eczema of the legs, with pityriasis of the scalp, in a patient who had never before suffered from any cutaneous affection. So far as I have been able to ascertain, there has been no similar observation recorded in the literature of this subject.

*The bullous form.*—Wigglesworth reports a case of a lady in whom bromide of potassium produced an eruption of bullæ which were somewhat acuminated, and varied in size from that of a pea to that of the end of the finger. Some

of the bullæ appeared to contain blood, and on rupturing exposed an ulcerated surface.[1]

In addition to the various forms of eruptive disorder from the use of bromide of potassium already noted, Veiel and others have described a squamous eruption, seborrhœic in character, preceding or coincident with the outbreak of acneiform lesions.

Clinical experience would appear to indicate that there is no essential difference in the pathogenetic influence of the various salts of bromine. Numerous observations have shown that the bromides of sodium and ammonium exercise the same irritating effects upon the skin as the bromide of potassium.

*Pathological anatomy.*—The pathological histology of the various lesions has not been carefully studied. Neumann made a microscopical examination of a pustular lesion in a child resulting from the ingestion of twelve scruples of bromide of potassium. He found the sebaceous glands, the hair-follicles, and the upper part of the corium to be the seat of the disease. The papillæ were increased in size, and the whole of the corium highly developed. The most marked feature of the changes was epithelial hyperplasia.

Seguin gives the histology of the lesion reported by him as follows:—Sections of the piece of tissue removed from ulcer showed great increase in the thickness of the rete Malpighii, with hypertrophy of the whole skin in places. The deeper layer of the skin and, to a certain extent, the subjacent connective tissue are infiltrated at certain points with young cells. The papillæ, hair-follicles, and sweat-glands do not appear to be the seat of any primary or important inflammatory change.[2]

*Pathogeny.*—Various theories have been advanced to explain the mechanism of the production of the bromine eruptions. From the fact that certain forms of bromine erup-

[1] The formation of bullæ, either with fluid or thicker contents, has been described by Neumann, Horrocks, Jacquet, and others. True bullæ, without more or less solid base, and with fluid contents, are, however, rare. When they occur it is generally in association with other characteristic lesions.—T. C. F.

[2] See also the papers by Waren Tay and Stephen Mackenzie, Colcott Fox and Heneage Gibbes, and Jacquet.—T. C. F.

tion, especially the papulo-pustular, appear in such a large proportion of all cases treated with the bromides, it is evident that idiosyncrasy, which plays so important a rôle in the production of other drug eruptions, does not figure prominently as a predisposing element. Without being constant, they are sufficiently common as to lead to the belief that they are, in a great measure, independent of individual predisposition, and may be developed in almost every case, provided the dose be sufficiently large and long continued. The changes which take place in the skin, like other symptoms of bromine cachexia, may therefore with propriety be classed among the exaggerated physiological effects of the drug, and it is plainly within the sphere of the nervous system that we must seek an explanation of these effects.

It is well known that the alkaline bromides are eliminated principally by the kidneys as well as by the salivary, lachrymal, and sudoriparous glands in a less degree.[1] It has been claimed that the sebaceous glands may also participate in this excretory action, and that the cause of the cutaneous disturbance observed after the internal administration of the bromine salts is the irritation attending the elimination of the drug through this channel. Plausibility is given to this hypothesis by the experiments of Guttman, who found bromine in the contents of the pustules.[2] On the other hand, Veiel and numerous other observers have failed to find the drug in any of the cutaneous lesions caused by its use, although it is always readily detected in the urine. While they do not deny the possibility of its excretion through the sebaceous follicles, yet they contend that the quantity thus eliminated is too minute to set up inflammation of the follicle, and thus give rise to acne by direct irritation. Clark and Amory regard bromine acne as a tropho-neurosis resulting from the direct action of the bromide upon the peripheral nerves, producing a derangement of the nutrition of the skin, of which the eruption is the outgrowth.

[1] Tilbury Fox, Shirley Murphy, Kaposi, and Colcott Fox have recorded cases of bromic eruption in infants nursed by mothers taking bromide of potassium.—T. C. F.

[2] Jacquet also detected bromine in the liquid secreted by patches of bromic eruption. He considers the eruption due to "péri-adénites sébacées et sudoripares."—T. C. F.

*Diagnosis.*—The appearance of the bromine rash is seldom attended with fever and other symptoms of constitutional reaction. As compared with other drug eruptions, it is more gradual both in its development and decline. The acneiform eruption is most often observed after the use of the drug in small doses has been continued for a long while. It increases in severity with the augmentation of the dose, and declines with its diminution. These characteristics have a certain importance from a diagnostic point of view, although there are few affections of the skin with which it could be confounded. In the maculo-papular form its brownish-red or copper tint might suggest syphilis. It is more liable, however, to be confounded with acne vulgaris, from which it may be differentiated by the absence of comedones, its development at periods of life which would exclude ordinary acne, and on parts of the body where this latter affection does not occur. Its association with other symptoms of "bromism," especially fœtor of the breath, and the presence of bromine in the urine, would leave no doubt as to the diagnosis.

### *Tests for Bromine and Bromides.*

Both bromine and iodine are liable to escape detection if an attempt is made to set them free in the urine. This is particularly the case with bromine. The reason is that both are prone to combine with some of the organic constituents of the urine, forming substitution compounds. To avoid error, it is best to proceed as follows:

Render the urine alkaline with potassa, evaporate it to a small bulk, transfer this to a crucible, and apply heat gently, until the contents are apparently dry and somewhat charred. Then cover the crucible and heat it to a *low* red heat until the mass is carbonised. Allow to cool; add water and boil for a short time, then filter. The filtrate, with washings, will now contain, besides other inorganic salts, any iodine or bromine in form of iodide or bromide.

Concentrate the filtrate, and add to a portion of it some disulphide of carbon, and afterwards *dilute* chlorine water, drop by drop, shaking after each addition. If bromine was present, the disulphide will assume a yellow or yellowish-

brown colour. Should it have a violet tint or colour, iodine is present. In this case the test is to be applied very slowly, and chlorine water added as long as the colour of the disulphide deepens, when this is to be removed and the test continued with a fresh portion of disulphide as above directed.

*Treatment.*—The main indication in the treatment of the cutaneous disorders caused by the internal use of the bromides is the suppression of the exciting cause. In certain conditions, however, the nervous symptoms of the patient may be of a nature to render the continuance of the medicine desirable, if not imperative. In order to realise the full therapeutic advantage of the drug, without its inconveniences, a number of adjuvants or correctives have been recommended. Arsenic has been recommended by Bartholow, Gowers, and others. Gowers found that five-drop doses of Fowler's solution caused the pustules of bromic acne to disappear in two weeks. This was evidently a *post hoc* conclusion, since experience teaches that the cutaneous eruption usually vanishes in this time without any treatment whatever. Sulphide of calcium is another drug which, on account of its well-known antipyogenetic influence, has been recommended to antagonise the tendency to the formation of pustules. Seguin found, however, that both arsenic and sulphide of calcium failed to influence the eruption in his cases.

Another expedient which suggests itself would be to give the bromide in doses just short of those sufficient to cause irritative effects upon the skin. But Falvet claims that the favorable results from bromide of potassium only begin to appear when an eruption of pimples appears on the skin of the face. Brown-Sequard thinks that the cropping out of an "acne-like eruption on the face, neck, and shoulders," &c., is an evidence that the bromide is proving curative, and he asserts that there is "a positive relation between the intensity of the eruption and the efficacy of the remedy against epilepsy."

CALX SULPHURATA—SULPHIDE OF CALCIUM.

The eruptive disturbances which follow the internal use of sulphide of calcium are chiefly of a pustular or furuncular character. It is only recently that the use of the drug has been revived, on the recommendation of Ringer, and the literature of its incidental effects is necessarily limited.

Hahnemann, quoted by Piffard, states that the calx sulphurata taken internally may cause vesicles, pustules, and furuncles on the healthy skin.

Alexander gives notes of three cases coming under his personal observation in which the ingestion of sulphide of calcium in varying doses produced a crop of furuncles distributed over the face, neck, forearms, wrists, and other portions of the body, accompanied in each instance with constitutional disturbance more or less severe. The dose in one case was eight grains three times a day, in the second one tenth grain, and in the third one quarter grain three times a day. The direct dependence of the eruption upon the use of the drug was inferred from the fact that amendment of the symptoms began in each case immediately upon suspension of the drug.

The following case came under my observation. A large, robust, florid-faced man, who had suffered for some months with successive crops of boils upon the back of the neck, was ordered pills containing each one quarter grain of the drug, one pill to be taken three times a day. The furuncular eruption began to disappear soon after commencing the use of the pills, but some days afterwards he called my attention to certain spots which had appeared on the lower limbs. On examination they were found to consist of a scattered eruption of pin-head to pea sized petechiæ, extending from the dorsum of the foot upwards above the knee. They were most abundant upon the calf, a few were seen upon the anterior surface of the thigh, none upon the trunk or upper extremities. I counted about one hundred altogether. Upon discontinuing the pills, the spots slowly disappeared in the course of ten days or two weeks.

As I was not positively certain of the relation between the drug and the eruption, I again ordered the pills in the

me dose. All doubt as to the causal connection was soon t aside by the reappearance of the petechial spots with most the same localisation as before.

In another case, in which I gave sulphide of calcium in ıe half grain doses for the relief of a furuncular affection the face and neck, there appeared a number of large ıstules upon the wrists, backs of the hands, and fingers. Whether this eruption was due to the influence of the drug, was a further manifestation of the same pyogenetic ten- ency exhibited in the furuncular inflammation, could not determined by further experiments, as the patient passed om my observation.

### CANNABIS INDICA.

The well-known physiological action of Cannabis indica on the sensory nerves of the skin, producing a marked egree of numbness and tingling, would lead to the infer- ıce that it possesses the property of causing cutaneous sturbances of an eruptive character.

The only case of eruption from this drug found in the erature of the subject is recorded by Hyde. The patient ıd taken one grain of the extract. The next morning the ırface of the scalp, face, ears, neck, trunk, and extremities, cluding palms and soles, was found covered with an erup- on of thickly disseminated vesicles, in size from a pin- ead to a split pea. The vesicles were developed upon the ımmits of papules; they were not grouped and did not alesce, and occasioned only a moderate pruritus. The uption subsided within a few days without treatment; ıe vesicles shrivelled up without bursting. After desicca- on the crusts fell off, leaving a transient pigmentation.[1]

### CANTHARIS.

The application of cantharides to the skin, in the form of ıtments, cerates, or as cantharidin, causes a sensation of ıgling and smarting succeeded by pain, redness, vesica-

[1] Aulde states that one of the symptoms of chronic poisoning with nnabis indica may be œdema of the face.—T. C. F.

tion, and the production of bullæ, which unite to form large blebs containing a pale yellow, serous, watery fluid, rich in albumen and fibrin.[1]

According to Trousseau, the skin about the blister, especially in persons of the dartrous diathesis, may become covered with vesicles, at first separate, but afterward confluent, forming a genuine eczema; pustules of impetigo may also appear. The eczema, at first limited to the region where the blister was applied, often extends by degrees in an acute form to the entire surface of the body. In persons of enfeebled constitution, ulceration, anthrax, furuncles, even gangrene of the affected surface may occur; or it may become the starting-point of erysipelas. Trousseau records the case of a female patient to whose thigh he ordered a flying blister for rheumatism; it was dressed with diachylon plaster. A few days later there appeared around the sore a vesicular eruption which soon invaded the entire surface of the body, causing high fever. This condition was replaced by a pemphigus which lasted some months. Pereira mentions a case in which the application of a blister to the pectoral region caused the development of echthymatous pustules, not only over the region of application, but also over the entire body.

In a case reported by myself, the introduction of cantharides by acupuncture for inflammation of the knee-joint caused intense inflammation of the penis and scrotum, with complete exfoliation of the epidermis of these parts; also strangury and hæmaturia.

Erythematous and papular eruptions affecting other parts than the genitals may follow the internal use of cantharides.

### *Tests for Cantharides.*

It is only when large doses of this drug have been taken, or when it has been taken for a certain length of time, that the presence of cantharidin can be demonstrated in the urine. The principal reliance is based upon the vesicating

[1] It is well known that troublesome pustulation may follow the application of a cantharides plaster. There is a model in Guy's Hospital Museum of a girl's breast inflamed by the application of powdered cantharides.—T. C. F.

power of the matter extracted, unless the quantity of cantharidin should be large enough to apply chemical tests, which is but seldom the case.

Cantharidin may be extracted by shaking a liquid containing it, after rendering it strongly acid, with chloroform. The suspected urine is concentrated to one fourth, rendered strongly acid by sulphuric acid, and then twice successively shaken with an equal volume of chloroform. The united chloroformic solutions are repeatedly shaken with water, then evaporated to dryness (or as far as possible), the residue heated with a little fixed oil of almonds, and a small piece of lint saturated with this oily solution applied to the breast, covered with a little court plaster. If notable traces of cantharidin were present, there will be more or less vesication.

### CAPSICUM.

Capsicum is stimulant and irritant to the skin and mucous surfaces. Its local application causes pain, itching, and redness, and, if sufficiently prolonged, produces vesication. Phillips says that applied to the skin, especially in a concentrated solution, capsicum is a powerful rubefacient, and will even blister if applied continuously.

Taken internally in large doses it produces a general glow of the surface, sometimes an erythematous eruption.

Allen states that teaspoonful doses of a solution of capsicum, taken at night, caused a papulo-vesicular eruption all over the body, with much burning and itching.

### CHLORAL.

The effect of the topical application of hydrate of chloral is irritant, and if the skin be deprived of epidermis, it

### CHINOLIN.

Draper found that in six out of twenty cases of typhoid fever chinolin caused an erythematous rash. It caused but little irritation, and faded in a few days, even when the remedy was discontinued.

Heuchen, of Upsala, observed the rash only in cases in which chinolin had no *abnormal* action on the temperature. He quotes a case seen by Laache in which an extensive rash occurred. Here the temperature sank and collapse followed.—T. C. F.

causes a sharp burning pain. Cantani pointed out that its external application produces erythema and vesicles surrounded by capillary hyperæmia. More recently Ritter has called attention to the fact that chloral has many points of superiority over cantharides as a vesicant. He found that powdered chloral sprinked over ordinary adhesive plaster slowly melted, and applied while warm to the skin, causes in three minutes a gentle heat, increasing in intensity for about three minutes until it is like a burn, then easing off, until at the end of ten minutes the parts feel free from pain. If the plaster be now removed, "the surface is found as effectually denuded as by a cantharidal plaster after six hours' application, although the discharge is not so great."

The eruptions which follow the internal administration of chloral[1] are comparatively infrequent, considering the extensive employment of the drug. It is claimed that, since improved methods of manufacture have been introduced, which insure a greater purity of the drug, from the elimination of certain deleterious chlorine compounds formerly present, the frequency and severity of incidental irritative effects have been much lessened. There is no doubt, however, that individual predisposition plays an important rôle in their production. While the type of the chloral rash is erythematous, a variety of eruptive phenomena have been observed from its internal use.

*The erythematous form.*[2]—A diffuse hyperæmia is the most common of the incidental effects of chloral upon the skin. It usually appears as a uniform redness or a bright flush upon the face, and may then successively affect the neck, chest, and extremities. Its places of predilection, after the face, are the extensor surfaces of the large articulations, knees, wrists, elbows, and ankles. It is a notable fact that while it almost always appears as a diffuse redness upon the face, upon other portions of the body it occurs in patches, or as dusky red spots with irregular borders, giving the skin a somewhat mottled appearance.[3] Ordinarily

[1] The so-called Érythème chloralique.—T. C. F.

[2] Winckel, cited by Martinet, and Mayor and Bouju have recorded cases in which the eruption was due to enemata.—T. C. F.

[3] Crichton Browne and others have frequently observed the "singular

it is transient in duration,[1] and is not attended with subjective sensations or constitutional disturbances.

The chloral rash is usually developed within a short time after commencing the use of the drug, rarely delayed longer than the tenth day. All observers have noted the fluxionary character of the hyperæmia; indeed, one of the most characteristic features of the eruption is the remarkable influence of hot drinks or a full meal in its production. Always after the ingestion of food, tea, alcohol,[2] &c., the rash becomes more intense and generalised. After suspension of the chloral even, the rash may continue to reappear for several days after each meal. The tendency to cutaneous irritation seems to remain latent until roused into activity by some stimulant to the vascular system. It then develops suddenly, remains out for a variable interval, one to two or three hours, and then vanishes, leaving no trace of its passage, except in some cases a slight furfuraceous desquamation.

In other cases the rash may appear as an inflammatory redness, which is strikingly suggestive of the scarlatina exanthem, and may spread over the entire surface of the body. This similitude to scarlatina is rendered more exact by the increased sensitiveness of the skin, the high fever, and the more or less abundant desquamation which follows.[3]

Köbner reports a case in which there appeared not a simple hyperæmic redness, but an erythema exudativum which spread over nearly the entire surface. The skin was more swollen and infiltrated than in scarlatina, to which it

tendency to flushing of the head and face." It is probably the condition referred to in some reports as "erysipelas." The face flushing often commences in patches about the lips, cheeks, and forehead. In cases where the eruption is generalised over the trunk and limbs the face becomes uniformly flushed, and the conjunctivæ and buccal and pharyngeal mucous membranes may be congested.—T. C. F.

[1] But, as in Bryant's case, may continue during the use of the drug.—T. C. F.

[2] The influence of alcohol has attracted special notice from numerous writers. Barbillion drew attention to the occurrence, in infants taking chloral day by day, of a fleeting patchy rash when some spirituous preparation of quinine, iron, &c., was added to the treatment. The ocular and buccal mucous membranes may be implicated.—T. C. F.

[3] The rash may be morbilliform (Saric and also Gontier, quoted by Bouju, Bryant, Middleton, &c.).—T. C. F.

bore a strong resemblance. It was attended with burning and itching, and, as the use of the chloral was persisted in for some time, it ended in desquamation in the course of four or five weeks.

*The papular form.*—Kirn reports a case of an eruption of papules situated upon red bases occurring upon the arms. Arndt reports a case in which doses of from two to five grains produced on the eighth day a papular eruption, consisting at first of scattered lesions which, later, coalesced into wheal-like patches. It appeared successively on the hands, forearms, chest, and face, and gradually spread over the whole body. It was followed by icterus. The eruption and the icterus disappeared on the suspension of the chloral. A papular eruption followed by jaundice was again developed a month later by giving the chloral in same doses.

Litten gives notes of the case of a girl who swallowed twelve and one half drachms of chloral at once. In addition to other symptoms of chloral poisoning, there appeared within twenty-four hours a general eruption of conical or globular papules of yellow colour, more numerously developed between the fingers and upon the face and breast. The eruption was quite itchy, and lasted about a week.[1]

*The urticarial form.*—Gauchet, Chapman, and others have observed a profuse eruption of urticarial wheals covering the entire surface of the body, attended with the usual subjective sensations of burning and itching. These eruptive phenomena appeared and disappeared with the renewal or cessation of the drug. Kirn reports cases of œdematous or urticarial swellings of skin over the whole body, which he ascribes to serous infiltration of the skin from stasis of blood.

*The vesicular form.*—A vesicular eruption which may develop into a pustular form sometimes occurs from the use of chloral. Kirn reports the case of a young woman in whom there appeared, on the ninth day of chloral treatment, an eruption in the form of groups of red spots which soon

[1] Gee also observed "a dusky red papular eruption, surrounded by a more diffuse redness of the neck and extremities, especially near the articulations, which were all more or less affected."—T. C. F.

became confluent. On the twentieth day of the treatment œdema of the cheeks, face, and eyelids appeared, and the skin presented at one time the appearance of a moist, at another of an impetiginous, and at still another that of a squamous eczema. The process of desquamation continued for many weeks, during which great sheaths of epidermis were cast off from all portions of the body. Profound disturbances of the skin nutrition were manifested by complete shedding of the nails of both hands and feet,[1] and by the sixth week large abscesses had formed about shoulders and armpits. The chloral was continued all this while, as the physician failed to recognise its association with the eruption. There was continuous fever, the temperature at one time reaching 106·7°.

*The petechial form.*—Browne reports a case in which the drug was given in twenty-grain doses three times a day. On the fourth day a redness, not effaceable by pressure, was observed over the skin of chest and shoulders. Two days afterwards the eruption had extended over the whole trunk as well as the limbs, deep red patches and livid spots alternating. The patient gradually recovered, desquamation occurring on the fifteenth day. Browne reports another case, in which forty-five grains of chloral, taken daily, produced on the nineteenth day a petechial eruption which rapidly became generalised. Patient died on twenty-sixth day. Kirn refers to a case observed by Monkton, in which the use of sixty grains of chloral daily produced on the fourth day a rash resembling variola with hæmorrhagic purpura. Two similar cases are reported by Pelman.

Reimer had observed, after large doses of chloral, lesions varying from circumscribed redness and swelling of the skin to deep ulcers, with formation of blisters on the trochanters, on the knees, tips of fingers, face, ears, and other parts,[2] and more or less extensive bedsores when the

[1] Prof. Smith called attention to the toxic condition, simulating ergotism, induced by small and long-continued doses. He noted superficial ulcerations, especially developed along the borders of the nails. This condition is also referred to in the 'Clinical Society's Report,' in association with a defective circulation of the hands.—T. C. F.

[2] In the 'Clinical Society's Report' a case of "pompholyx" was attributed to chloral by Humphrey, of Aylesbury.—T. C. F.

patient has lain long in one position. Reimer refers these changes to anomalies of the circulation brought about by the paralysing influence of chloral upon the vaso-motor centres.[1]

*Pathogeny.*—A number of theories have been offered in explanation of the irritative effects of chloral upon the skin. The striking analogy which the chloral rash presents with the erythema provoked by copaiba, both in its appearance and in its predilection for the articulations, has suggested the hypothesis that it may be due to the direct action of chloral upon the glands of the skin. No such mode of elimination has been demonstrated in the case of chloral, and such an hypothesis is clearly untenable. Other authors regard it as the result of chronic blood-poisoning with determination of the morbid phenomena towards the cutaneous surface. However probable this theory may seem in the exceptional case recorded by Kirn, in which large doses were continued for many weeks, resulting in profound disturbances of nutrition, yet it is manifestly inadequate to explain the more common and characteristic forms which often promptly appear even after small doses.

The theory most in accord with a rational interpretation of the pathological phenomena is based upon a recognition of the influence of chloral upon the vaso-motor nerves. According to this theory, the chloral erythema is an angio-neurosis caused by a paralysis of the vaso-motor centres of the head and neck. Whether this is due directly to an impression of a particular nature exercised upon the nerves of the stomach and the ganglia with which they are connected, or whether it is caused by an action of the drug absorbed into the circulation upon the nerve-centres, is a matter for future inquiry. The urticarial and purpuric forms may also be regarded as an expression of neurotic disturbance.

[1] In one of Crichton Browne's cases the lips and buccal mucous membrane were red and raw-looking, the gums spongy, the tongue blistered and ulcerated; in another the lips were raw and the tongue fissured and thickly coated. Bathurst Woodman mentions ulcers of the cornea, ulcers of the tongue, boils, and carbuncular affections as possibly due to chloral given to children.—T. C. F.

*Diagnosis.*—Little difficulty should be experienced in the diagnosis of the chloral eruption. From measles and scarlatina it may be differentiated by the absence of fever, catarrhal symptoms, characteristic throat and tongue, &c.[1] It may be confounded with the erythema produced by belladonna, copaiba, and quinine respectively. The belladonna rash is almost always accompanied with mydriasis, dryness of the fauces, &c. The chloral rash has special features of its own, such as the absence of subjective sensations, its liability to development after the ingestion of alcohol or a full meal, which serve to distinguish it.[2] The peculiar odour exhaled in copaibic eruptions is always of diagnostic value.

### *Tests for Chloral.*

If chloral is to be detected in urine, the latter is mixed with about one fourth volume of alcohol, then rendered neutral, if necessary, by either carbonate of magnesium or tartaric acid, as the case may be, and distilled until only a syrupy residue remains. The distillate now contains the chloral. This is recognised by its products of decomposition, viz. chloroform and formate of ammonium (or of other alkali), when the solution is treated with an alkali. The distillate is, therefore, rendered alkaline with soda, and again distilled. The new distillate will contain the chloroform, which is identified as shown below. The formate is recognised in the residue by the fact that the latter promptly reduces nitrate of silver to a metallic state—a portion of the residue, when heated in a test-tube with solution of nitrate of silver, producing a brilliant metallic mirror.

[1] It has already been pointed out that fever and a congested throat may occasionally be present, and there may be running from the eyes, with conjunctival congestion.—T. C. F.

[2] Itching is present occasionally, even to a considerable degree, *e.g.* Husband's case. The sites attacked and the order of evolution from the face, neck, chest, to the great articulations are of some importance. Further, there is the evanescence of the rash and its reappearance when the chloral is readministered, and finally the dyspnœa, palpitation, &c., usually provoked. Bouju failed to confirm Barbillion's observation that the breath acquired a special ethereal odour. Watson and Hutchinson record cases in which the eruption was confined to the hands.—T. C. F.

The chloroform in the distillate is recognised by converting it into isonitril—a body of a penetrating and disagreeable narcotic odour. This is accomplished by adding to the aqueous solution suspected to contain chloroform some alcoholic solution of potassa, then a drop or two of aniline, and warming. The peculiar odour of isonitril or phenyl-isocyanide will make its appearance. The same reaction is afforded by iodoform, but in the case of chloroform no iodine can be set free as in the former (see Iodoform).

*Treatment.*—No special treatment is required for the relief of the irritative effects of chloral. No drug given in combination appears to exert a corrective influence. The eruption disappears spontaneously soon after the discontinuance of the drug.

CHLORALAMIDE.

Pye-Smith observed a rash apparently due to chloralamide in a brewer's cellarman, aged forty, suffering from aortic valvular disease and aneurism, and slight congestive albuminuria. The patient took either 40 or 80 grains every night, with one exception, from December 1st to 13th. Then his eyes were red and watered, and a rash appeared on the face, neck, and chest, and rapidly spread till the whole surface was covered with a diffuse hyperæmia, which was, however, punctate. A few vesicles formed in places. There was some febrile reaction, hyperæmia of the mouth, and running from the nose. The rash began to fade on the fifth or sixth day, and ended in free desquamation.—T. C. F.

CHLOROFORM.

Dr. Dudley Buxton has kindly given me the following note:

"The rash which accompanies the onset of anæsthesia when induced by chloroform or, more particularly, by ether, is erythematous in nature. It appears upon the neck and chest usually in patches which extend and coalesce, giving, especially with ether, a deep red coloration over the inter-mastoid and subclavicular regions. It usually is accompanied by a profuse perspiration, but the two conditions are not locally coterminous. The rash usually disappears after a few minutes, leaving, as a rule, a blush behind it which is less discrete, and often extends over the arms. The form of the rash varies in individuals, being sometimes almost punctate, but this always leads to a coalescence and blotchy arrangement later. The rash is not present in all persons who take anæsthetics, nor can one say that one sex, age, or diathesis predisposes to the appearance."

Morel-Lavallée records three cases in which purpuric spots were formed under observation during the early stage of administration of chloroform by inhalation (Crocker).—T. C. F.

CINCHONA—QUINIÆ SULPHAS.

The various eruptions which have been grouped under the general term "quinine exanthemata" follow indifferently the exhibition of any of the preparations of cinchona. Since the introduction of the alkaloid to the profession in 1820 it has been almost universally employed to the exclusion of the crude bark, which fact will explain the far greater number of eruptions recorded under this head. While it is presumable that cutaneous disturbances have frequently followed its use from the time of its first introduction, it is worthy of note, that prior to 1870, with the exception of five cases under the care of M. Bouchut in the Hôpital de la Pitié, in which there was observed an erythematous eruption from the ingesting of quinine, no such results have been recorded.

Although the casual contact of quinine with the healthy human skin does not act as an irritant, yet it has been observed that workers in quinine factories are subject to eruptions of various kinds. Evidently these effects are not due solely to external irritation, but in a great measure to absorption of the quinine emanations. Chevallier called attention to the fact that the fabricants of quinine often suffer from affections of the skin, characterised by the development of papules, vesicles, and pustules on different parts of the body, particularly the hands, arms, and legs. Bergeron and Proust have made a careful study of these eruptions, and describe them as habitually sudden in their development, involving most frequently the hands, forearms, internal surface of the thighs, and the genital regions. The eruption is usually eczematous in character. Upon patches of reddened skin are observed numerous vesicles, confluent and exulcerated at certain points; in other parts, the serosity has dried up and given place to scales and crusts. Instead of ordinary vesicles there may be larger lesions resembling the veritable bullæ of pemphigus. Sometimes quite extensive surfaces are seen deprived of epidermis, red and œdematous. The face may be swollen and covered with crusts

of eczema, the eyes weeping and injected. This condition readily subsides in the course of a few days under the influence of emollients, protectives, &c.[1]

Monk found, upon passing a current from ten Grove's elements through the body, the electrodes having been moistened with a solution of quiniæ sulphatis, that the surfaces acted upon became first dry and anæmic, but in the course of a few hours they became hyperæmic and covered with a number of pin-head sized extravasations of blood, which remained after the hyperæmia had subsided.

Delioux de Savignac reports a case in which the application of a pomade containing sulphate of quinine produced intense pruritus and an eruption of lichen. Quite recently, I observed an urticarial eruption in a young lady patient suffering from phthisis, resulting from the topical application of a solution of one drachm of quiniæ sulphatis in one pint of alcohol, which I had ordered for the relief of night sweats. The wheals were abundant, and distributed over the entire surface of the body, and they continued to recur for two or three days, until I ordered the application to be discontinued, after which they promptly subsided.[2]

Taylor records a case of a young woman in whom a well-marked dermatitis was developed every time she took quinine internally. She began to use a "rum and quinine" hair tonic, and wherever the quinine preparation came in contact with the skin it caused a dermatitis identical with that caused by the ingestion of the drug. A similar case came under Otis' observation.[3]

According to Aitken, irritability of the skin, extensive erythema, ulceration, and abscesses at the point of injection, with painful and inflammatory nodules of the subcutaneous

[1] It is altogether exceptional for a workman to acquire an immunity. Persistence in exposure usually induces increasingly grave consequences. Many cases of extreme susceptibility are mentioned.—T. C. F.

[2] Briquet, quoted by Bergeron and Proust, observed a general erythematous eruption after a sulphate of quinine bath.—T. C. F.

[3] Ringer also mentions the case of a patient in whom quinine produced a violent urticaria, with great swelling of the face. A quinine hair-wash brought out a crop of urticaria on her head, and a quinine tooth-powder caused her lips and gums to swell. See also p. 469.—T. C. F.

cellular tissue, are not infrequent results of the hypodermatic injections of the salts of quinine.[1]

The eruptions which follow the ingestion of quinine are multiform in character. The prevailing type of the quinine exanthem is erythematous, but every form of elementary lesion—macules, papules, wheals, vesicles, bullæ, pustules, purpura, &c.—have been observed as the direct result of the administration of this drug.

In a study of the eruptions produced by quinine, published in the 'New York Medical Journal,' March, 1880, I gave the result of my examination of sixty cases of quinine eruptions published within the previous ten years. Analysis of these cases shows that the different forms of the eruption were represented as follows:

*The erythematous form.*—In thirty-eight of the sixty cases referred to the general character of the eruption was erythematous. It was further described as "scarlatinal," "scarlatinoid," "bright red," "measly," "rubeolous," "papular," "erysipelatous." In most cases it appears as an efflorescence of a bright, vivid hue, disappearing on pressure, and closely resembling the rash of scarlatina. Usually it first shows itself upon the face and neck, but soon becomes diffused over the whole surface of the body; in exceptional cases it may not become generalised, or it may appear in the form of distinct red spots, which become confluent and patchy,[2] and the coloration may exhibit a darker hue, resembling that of measles. The eruption promptly disappears upon the discontinuance of the drug, and is usually followed by desquamation of a branny or lamellar character. In one case desquamation continued for three months.[3]

[1] Köbner attributes these results to the irritating effects of the older vitriolic preparations.—T. C. F.

[2] Erythematous patches and discs, described as roseola, are mentioned by authors (Bouvard).—T. C. F.

[3] In a case recorded by Hagan an infant was subject to attacks of erythematous eruptions, urticaria, &c., for three years, so that his skin became thickened and scaly. The nature of the case was unsuspected for a long time, but it was eventually discovered that the mother was in the habit of dosing the children frequently with quinine, as a preventive of various ailments. When the quinine was discontinued the eruptions ceased, the

*The urticarial form.*—The eruption may present itself with the typical wheals of urticaria. In twelve of the cases the eruption was described as "urticarial" with "œdema," "puffiness of the face," &c. In this class of cases there is more or less œdema of the face, and the subjective sensations of burning, tingling, and itching are quite distressing. The general features of the following case are typical of this form. In November, 1875, I had occasion to prescribe sulphate of quinia, in two-grain doses, to a gentleman suffering from some bronchial trouble. He took the first dose late at night on going to bed. Soon after he began to experience a feeling of oppression in his chest and a sensation as if his throat were filling up, accompanied with the most intolerable burning and itching over the whole surface of the body. When I saw him the face was œdematous, and the entire surface was hyperæmic, and covered with wheals, most abundant about the face and neck. These symptoms subsided during the day, and I advised him to take another dose of the quinine the succeeding evening. Its repetition was followed by a redevelopment of the urticarial rash, and I now suspected that the two might stand in the relation of cause and effect. I gave no more quinine, and his cutaneous troubles speedily vanished. The patient, who was a retired physician, was as much surprised at these unusual effects of the medicine as myself. He had formerly practised medicine in a malarial district, and had been accustomed to take large doses of quinine without experiencing anything beyond its ordinary physiological effects. Two years later he suffered from malarial trouble. Remembering his former unfortunate experience, he did not at first take quinine, but, curious to test his vulnerability, he finally decided to try it in one-grain doses. In less than an hour after taking the first dose he had a violent attack of urticaria, which affected the mucous membrane of the throat and fauces, as well as the entire surface of the body.

*The papular and vesicular forms.*—In a few cases, the eruption was described as papular[1] or vesicular in character.

skin was quickly restored to its normal condition, and the boy was proved to have the idiosyncrasy towards quinine.—T. C. F.

[1] In a case described by Buch reddish, somewhat raised, erythematous

In a case reported by Denk the eruption presented the features of an eczema. The papules developed upon an erythematous or scarlatiniform base were transformed into vesicles. The vesicles, pin-head in size, were more abundantly distributed about the neck, chest, and axillary region. After the drug was discontinued the vesicles dried up, and desquamation occurred in scales or large lamellæ. Reveillod ordered a patient seventy-five centigrams of quinine three times a day. The third day he complained of intense burning and itching on palms, forearms, thighs, and feet, which was followed by a erythemato-papular eruption. The patient had formerly worked in a quinine factory, but had been compelled to quit his employment on account of the irritating effects of the quinine. In Heusinger's case an eruption resembling erythema exudativum multiforme, attended with œdema of the lids, appeared on the face of a lady after taking one half grain of quinine. On another occasion one and one half grains of quinine produced an eruption of herpetic vesicles on the cheeks of the same patient.

Otis relates a case in which a vesicular eruption, some of the vesicles being larger than a pea, had been produced and reproduced by the internal use of quinine. In one instance two or three grains produced a severe eruption resembling that from ivy poison. The same followed the employment of a hairwash, of which quinine was an ingredient.

*The Petechial form.*—A number of cases of purpuric eruption from quinine have been recorded. Moneret (cited by Deschamps) observed small ecchymoses spread over the surface of the abdomen of a patient who had taken quinine. Briquet saw in a patient taking three grams of quinine a day a large ecchymosis develop upon the buttocks and external surface of the thigh, and at the same time a petechial eruption coincident with a sanguinolent diarrhœa. I have observed a purpuric eruption in the case of a boy twelve years of age suffering from malaria, who was ordered by his physician the following treatment :—Five three-grain pills of quinine the first day, four the second, three the third, two

papules, the size of a pea, and free from irritation, appeared on the legs, and on readministration of the quinine all over the back.—T. C. F.

the fourth, and one the fifth day. Before he had completed this course, an eruption of purpuric spots appeared on the body, more abundantly distributed on the lower extremities. They disappeared in the course of ten or twelve days after discontinuance of the medicine. Wigglesworth observed an eruption of non-elevated, irregularly circular patches situated upon the forearms and ankles. They were attended with burning and itching, and were painful on pressure. The spots appeared one hour after taking a one-grain pill of quinine, and, under the continued use of the pills, until twelve were taken, the lesions increased in size and number, and became well-marked hæmorrhagic patches. Vepan, cited by Jeudi di Grissac, reports four cases in which an eruption of petechial spots occurred over the whole body from the use of comparatively small doses of quinine. In a case of a lady who took first 0·1 and later 0·15 gram, the eruption increased in violence and extent with the increase of the dose. In this case the purpura was accompanied with bleeding from the gums and sanguinolent stools.

Gauchet reports a case in which the intolerance of quinine was so absolute that small doses, only ten centigrammes continued for four days, produced purpura with buccal hæmorrhage, principally from the gums. The petechial spots were abundant and generally distributed. In this case Gauchet gave quinine in opposition to the wishes of the patient, who stated that she had taken it before and that it always caused her to spit blood.[1]

*The bullous form.*—This form is comparatively rare, but the possibility of its occurrence is well authenticated. M. Panas, cited by Bergeron and Prost, affirms that the administration of large doses of quinine (two or three grams, as is the custom in Algiers and Greece) provoked an eruption resembling the bullæ of pemphigus.

Fowler reports a case in which four grains of bisulphate of quinine produced an eruption of bright-red patches, varying

[1] Köbner records a case of hæmorrhages into the skin and from the bowel which recurred after the subcutaneous injection of quinine in a child. He refers to other instances of tympanic and intestinal hæmorrhage following the use of quinine. Hæmaturia, epistaxis, and bleeding from the tonsils have also been recorded on several occasions.—T. C. F.

in diameter from one half to two inches, over wrists, forearms, knees, and ankles; twenty-four hours later the spots came to have a mixture of bluish and yellow colours, and in some of them very considerable sacs of fluid had collected beneath the epidermis. The bullæ soon shrivelled and disappeared, and the cuticle peeled off, leaving dark, bruised pigmentations, which did not disappear for three months. The patient has had a similar experience seven or eight times before. On this occasion the amount taken was only one half of a grain.

*The gangrenous form.*—In the case above quoted from Briquet, the ecchymotic patch became gangrenous. In one case, reported by Professor Schuppert, six-grain doses produced an intense localised dermatitis with commencing gangrene of the scrotum. In one of Professor Köbner's cases, quinine always produced an erysipelas of the scrotum. In several cases the special tendency to irritation of the skin of the genital parts is noted.

In many of the cases reported several successive outbreaks of the eruption occurred, because the physician either repeated the dose without suspecting the causal association of the drug and the skin disease, or did so because he wished to satisfy his own mind as to the patient's susceptibility. The occurrence of one attack seems to confirm and intensify this morbid susceptibility.

It is worthy of note that what may be called the idiosyncratic intolerance of the drug may be an acquired peculiarity. In a number of cases, my own among them, the patient was previously accustomed to take large doses of quinine without any unusual effects upon the skin. Observations are not wanting which would seem to demonstrate the hereditary character of this peculiar susceptibility in exceptional cases. King reports the case of a lady who had vivid bright-red efflorescence developed over the whole surface of the body after taking five grains of quinine. She stated that her father, as well as her sister, were always affected in the same manner after taking quinine. In a number of cases, where preparations of the bark were given, the physician, thinking that the irritant effects might be due to some adulteration, substituted the alkaloid, with a repetition of the

same effects. In a majority of the cases, what may be regarded as small doses—one or two grains—were given. The subjects of these observations were mostly females. The greater fineness of the skin and its more exquisite sensibility in women would explain its relatively greater susceptibility to irritant action.[1]

*Pathologeny.*—One theory of the mechanism of the production of the quinine exanthem is that the drug may act just as irritating articles of food sometimes do, by stimulating the sensory nerves of the gastric mucous membrane, producing reflex dilatation of the cutaneous vessels. While this explanation may apply to the lighter and more transitory forms, such as the erythematous and urticarial, it is manifestly inadequate to cover the severer forms. Another theory is, that the sweat glands have an elective affinity for the drug, and its attempted elimination through this channel causes local irritation.[2] While it is not probable that the drug acts specifically upon any one of the constituent elements of the skin, we can readily understand that it may exert a direct irritant effect through the blood upon the vaso-motor and trophic centres, causing disorders of capillary circulation, of which the eruption is but the outgrowth. In purpuric cases there may be diminished vitality of the cutaneous vessels from disordered innervation, permitting transudation of blood through their weakened walls.[3]

*Diagnosis.*—The quinine exanthem derives its chief clinical importance from its close resemblance to the rash of scarlatina. This resemblance is rendered more striking from the congestion and swelling of the mucous membrane of the throat and fauces, and the subsequent desquamation, which may be more of less complete, and may last from a few days to several weeks. In one case, reported by Dr. Pfluger, there was exfoliation of the epidermis in large lamellæ, giving a complete cast of the fingers like a glove.

[1] Some authors suggest that the nervous temperament has a predisposing influence.—T. C. F.

[2] Quinine is said to be eliminated in all the secretions.—T. C. F.

[3] It may be perhaps useful to note that Porak (quoted in the 'Brit. Med. Journ.,' August 31st, 1878) has proved the passage of quinine by the placenta from the mother to the infant.—T. C. F.

When the eruption is accompanied with fever and high temperature, as in the cases of Professor Köbner and two other reporters, its similitude to scarlatina is so perfect as to deceive the most skilful and experienced physicians; but these cases are quite exceptional. The differential diagnosis is usually easy, from the absence of fever and high temperature, the sudden development of the rash, and its rapid subsidence upon the suspension of the medicine.[1] The presence of quinine in the urine, which may be readily detected by simple and easily applied tests, will at once decide the nature of the exanthem.

*Tests for Quinine and other Cinchona Alkaloids.*

The principal alkaloids of cinchona bark, used in medicine, are quinine, quinidine, cinchonine, and cinchonidine. All of these are eliminated promptly by the urine, without any apparent chemical change. The separation of these alkaloids from the urine is comparatively easy, but their separation from each other, and sometimes their identification, is connected with difficulties, particularly if attempted by inexperienced hands. However, the recognition of quinine and quinidine is comparatively easy. For this purpose, the urine is evaporated to a small bulk, then rendered alkaline with soda, and agitated with chloroform, which will dissolve the quinine, quinidine, and cinchonidine, and but little cinchonine. (The latter may be subsequently shaken out by a mixture of four volumes of chloroform and one volume of alcohol.) The chloroformic solution is mixed with a few drops of water and evaporated to dryness. A proportion of the residue is then placed on a watch-glass, a few drops of chlorine (or bromide) water poured upon it, and then a drop of water of ammonia, whereupon an emerald-green

[1] Itching, sometimes intolerable, is recorded in many of the cases of scarlatiniform eruption. The primary seat of evolution of the rash seems to vary. There is a remarkable proneness to recurrence. In addition to febrile movement there may be marked general disturbance, dyspnœa, &c. Occasionally the eruption may be more localised. In a few cases the swelling of the face or limbs has been so marked as to suggest erysipelas. More than one author also mentions some transitory joint-swelling, which might delude the observer (Glax, Buch, Posner).—T. C. F.

colour will make its appearance if quinine (or quinidine) was present.

Treatment is hardly ever necessary for the cutaneous disorders caused by quinine, since they spontaneously disappear on withdrawal of the offending agent. A simple protective dusting powder will relieve the subjective sensation of heat and itching which commonly characterise the erythematous and urticarial forms.

A number of expedients have been suggested to prevent the irritating effects of quinine upon the skin. Lightfoot observed the rapid disappearance of the quinine eruption following the administration of twenty-five drops of tincture of hyoscyamus and sponging the body with alcohol. Hydrobromic acid, it is claimed, exerts a remarkable influence in counteracting the untoward effects of quinine.

### CONIUM.

Conium in large but not toxical doses, according to Stillé, sometimes produces an erythematous or papular eruption upon the skin in conjunction with injection of the eyes, diaphoresis, and other characteristic symptoms.

Dierbach, quoted by Piffard, states that diaphoresis, erysipelatous inflammation, bluish spots, or a rosaceal eruption may follow the internal use of this drug.

### COPAIBA AND CUBEBS.

The eruptive disturbances caused by copaiba and cubebs are generally recorded together under the head of "balsamic eruptions."

Since these two drugs are so often given in combination, it would be difficult to differentiate the part played by each in the production of the cutaneous phenomena.

It will be most convenient, therefore, to study their incidental effects upon the skin in the same connection; it must be noted, however, that the two drugs are not equally

### CONDURANGO.

J. E. Guntz records a case of furunculosis following the internal use of condurango.—T. C. F.

endowed with exanthematogenic properties; while the eruptions produced by cubebs are quite rare, those which follow the ingestion of copaiba are comparatively frequent. They were first described by Montègre in 1814, and afterward by Ricord, ten years later, under the designation of *érythème des resineux*. Bazin differentiated the clinical features of the balsamic eruptions, and to his admirable description little has since been added.

In some cases, the eruption appears soon after the administration of the drug; in other cases, not until after it has been continued for some days, almost always by the eighth day.

The copaiba rash manifests a predilection for certain regions, as the wrists, ankles, knees, hands and feet, breast, and abdomen, sometimes it is general, occupying the entire surface of the body. A number of eruptive elements have been met with, but erythema and papules are by far the most common.

*The erythematous and papular form.*—This is characterised by rosy or bright-red spots, the hyperæmia disappearing on pressure. Its favourite seat of development is around the articulations. The patches are usually rounded, sometimes irregular, not elevated above the surrounding skin, separated from each other by interspaces of perfectly normal skin, and sometimes coalescing, forming patches of considerable size. Certain observers have described miliary and scarlatina-like eruptions with œdema of the subcutaneous cellular tissue. It is accompanied with itching, which may be very intense. It usually recedes promptly with the cessation of the medicine, the spots gradually fading and disappearing with slight desquamation. If the use of the drug be continued, the hyperæmic spots may develop into papules, or the rash may be papular from the first. Berenguier describes a case of eruption from cubebs, in which the lesions were miliary, but uniting in many places, forming finger-nail sized elevations above the surface of the skin. The eruption spread over the face, arms, and trunk, less abundant over lower extremities. It disappeared with a slight branny desquamation in a few days after stopping the use of the medicine. Weiss gave a young man twenty

grains of cubebs, which produced high fever, and an eruption so closely resembling roseola that it was deemed necessary to take suitable precautions to prevent the spread of the infection. The eruption disappeared in three days. A second similar dose produced precisely the same phenomena.[1]

*The urticarial form.*—The rash may commence as an urticaria, or wheals may be developed secondarily upon an erythematous surface. In a case under my observation, the rash on the first day presented the aspect of a roseola affecting only the seats of predilection indicated above. Two days later, the medicine having been continued, almost the entire surface of the body was erythematous and covered with large rosy-red wheals, accompanied with more or less œdema of the face. The eruption was most abundantly developed upon the back, shoulders, and buttocks. Upon the legs the eruption was petechial in character. The eruption disappeared with the cessation of the medicine. Two weeks later the medicine was again given, by way of experiment, with the result of reproducing the same eruptive elements.

[1] The so-called *Roseola balsamica* or *balsamic erythema* arising from the ingestion of copaiba is probably the drug eruption most widely known in the profession, as it is frequently seen. My colleague, Dr. Murrell, who was administering the drug for chronic bronchial catarrh, lately sent me quite a number of cases. The shades of colour on different parts of the body and the intensity of evolution and amount of eruption vary. In all the cases I have seen the rash evolved as discrete, tiny, erythematous punctæ or papules, apparently seated at the follicles, and tending to group together (morbilliform) into patches, which may become confluent and resemble erythema multiforme. If the hyperæmia be very intense vesicles may occasionally form here and there, or the patches become urticarial. The face may be flushed, the conjunctivæ injected, and in some cases there may be considerable œdema of the skin. The degree of irritation varies, but is sometimes intense. There may be considerable febrile reaction and signs of irritation of the gastro-intestinal, respiratory, and genito-urinary tracts. Diday said toleration might be established.

This is an eruption which especially raises the question whether the various symptoms are due to the elimination of the drug. Gubler explains the eruption by the passage of the volatile oil by the sweat glands. Bartholow attributes some, at any rate, of the urticarial conditions to gastro-intestinal irritation.

In Neligan's work on 'Diseases of the Skin' is an account of a mother who was taking copaiba and suckling her child. Both were attacked with urticaria.—T. C. F.

*The vesicular form.*—Rayer reports a case in which the administration of copaiba and cubebs was followed by an eruption of vesicles similar to those of eczema. It consisted of numerous pin-head sized vesicles filled with transparent fluid, developed principally upon the wrists, elbows, ankles, and knees. The skin was red, hot, and swollen, presenting a condition analogous to that of eczema rubrum.

*The bullous form.*—Hardy has reported a case of pemphigus-like eruption following the use of copaiba; the drug first produced an urticarial eruption, discrete upon the face and chest, confluent upon the limbs, attended with intense itching, which disappeared in four or five days after the discontinuance of the copaiba. After several days administration of the drug a second time, there appeared an eruption of large, irregular, incomplete bullæ, which readily ruptured, followed by desquamation lasting six weeks. The eruption came out in successive crops—the duration of each bulla was about six days.

In 1874 I was called to a patient who had been taking copaiba, whose entire body was covered with a patchy erythematous eruption, very itchy; the spots were discrete except around the ankles, in which location there was a belt of vivid diffuse redness two or three inches in width, completely encircling them; over this reddened zone there were a large number of bullæ, some of them discrete, others confluent. The development of the bullæ in this locality was attributed to the pressure of elastic gaiters.

*The petechial form* of copaiba eruption is usually associated with the erythematous and urticarial. Hyde has seen the rash of copaiba occur in dark mulberry-red patches. Judd described a copaiba eruption resembling the bite of insects.

Mauriac describes an eruption from copaiba and cubebs presenting unusual features. After the eruption had lasted several days, the spots upon the extremities, especially upon the forearm and wrists, displayed centres of ecchymotic redness surrounded by pale-red circles, which in their turn were circled in other circles of dark red, each patch measuring from two to three centimetres in diameter. On the lower extremities there were multitudes of pin-head sized petechiæ.

*Diagnosis.*—The copaiba rash derives its chief clinical importance from its similarity to the erythematous syphilide and the rash of the eruptive fevers, especially rötheln, when the papular element predominates. The diagnostic differences in configuration, colour, localisation, exhalation of resinous odour of the drug, &c., need only be alluded to.[1] The odour of the essential oil of copaiba, of cubebs, of juniper, and of turpentine (pure) can generally be distinguished. This may, however, be done with greater certainty if the urine is distilled to a syrupy consistence, and the distillate shaken with petroleum ether of as low boiling point as possible (f. i., rhigolene). On spontaneous evaporation of the latter, the odour of the essential oil may usually be recognised, when the last traces of the solvent are volatilised. If this movement is missed, the essential oil itself may volatilise and thereby fail to be identified.

### DIGITALIS.

The external application of the fresh leaves of foxglove in the form of an ointment excites an irritation of the skin which may result in an erythema, or an eruption papular in character. The production of an exanthem from the ingestion of digitalis has been but seldom observed. Behrend, quoted by Hyde, refers to macular and maculo-papular eruptions succeeding its use.

Traube reports two cases in which affections of the skin resulted from the internal use of digitalis. In one case the patient had taken a quantity of the infusion representing nearly sixty grains in the course of two days. Four days after the last dose there appeared an erysipelatoid affection of the face, which terminated in an excessive ragged desquamation a few days later.

In the next case sixty-one grains had been taken in the form of an infusion in the course of five days. Four or five days after the last dose an eruption of prominent reddish papules appeared on the body, backs of hands, and forearms. These papules coalesced, forming large patches elevated

[1] Arthur Cooper records a case in which the balsamic eruption and erythematous syphilide were co-existent.—T. C. F.

above the surface of the skin. The next day new patches appeared upon the upper arms and neck. The exanthem disappeared in a few days, desquamation in large flakes occurred some days later on the body and extremities.

It is a noteworthy fact that the eruption appeared in each case four days after the suspension of the medicine, which is in harmony with the well-known cumulative effects of the drug upon other organs when not rapidly eliminated from the vascular channels.

Schuchardt reports a case where a similar form of eruptive disturbance, involving the entire surface of the body, was twice developed by the use of digitalis.

A case in which the irritant action of digitalis upon the skin was singularly shown, came under my observation a few years ago. The patient had been taking infusion of digitalis in active doses, with acetate of potash, for partial suppression of the urine. After a few days of this medication, there appeared an erythematous efflorescence over the entire surface of the body, which the family of the patient thought was scarlet fever. The next day, the medicine still being continued, the whole surface was covered with an urticarial eruption. The wheals appeared as large prominent plaques, elevated considerably above the surface, and intensely itchy. There was œdema of the face, puffiness of the eyelids, high temperature, and considerable constitutional disturbance. The eruption began to disappear in the course of two or three days after cessation of the medicine. Desquamation in large flakes continued for several weeks. There was complete alopecia of the scalp and shedding of the nails of the fingers and toes. Albuminuria was constantly present for some time after the attack.

### DULCAMARA.

The most characteristic incidental effect upon the skin produced by the ingestion of this drug is an increased sensitiveness, and the appearance of an erythematous condition. Urticarial and "red-scaly" eruptions have also been recorded from its use.

## ERGOT.[1]

The condition called "ergotism" may result from the internal administration of the drug in medicinal doses, or from the consumption of bread or other farinaceous food strongly impregnated with the diseased rye. Changes in the skin from the ingestion of ergot are comparatively rare, and only supervene upon its long-continued use. A vesicular eruption upon the skin with petechiæ has been observed, also a pustular and furuncular inflammation; sphacelus and circumscribed gangrene may occur on parts distant from the centres of circulation.[2]

The group of skin lesions comprehended under convulsive and gangrenous ergotism will not be considered here, since they are phenomena caused by consumption of food infected with ergot, and rarely result from the use of the drug in medicinal doses.

The hypodermic injection of ergotin is usually followed by more or less intense symptoms of local reaction. At the point of puncture there generally results a painful black unsightly swelling. These nodules are exceedingly sensitive, and may persist for some time. A phlegmonous inflammation around the point of injection not infrequently results. Carrying the instrument deep down into the subcutaneous tissues does not prevent the formation of these nodular infiltrations.

[1] In connection with ergotism, reference may be made to somewhat analogous diseases probably associated with diseased bread-stuffs, viz. the mysterious epidemic diseases acrodynia, pellagra, and the affections occurring in India from the consumption of diseased grain or some of the various leguminous seeds known generically as Dâl. Hirsch's 'Handbook of Geographical and Historical Pathology' may be consulted for references.—T. C. F.

[2] Reformatski, in the serious epidemic of ergotism occurring in Eastern Russia, 1889-90, observed trophic changes affecting the hair and nails. In the Frankenberg epidemic in 1879 slight analgesia of the anæmic fingers was observed, also bullæ, miliaria, eczema, boils, urticaria, and loss of nails and scalp hair.

Meadows records a case in which intoxication and redness and swelling o the face, eyelids, and right arm recurred on three occasion in a woman after the administration of ergot. He refers to another similar case.—T. C. F.

### FERRUM—IODIDE OF IRON.

The most common cutaneous disturbance observed from the internal use of iron is an acneiform eruption. Trousseau says that it is more frequently observed in women, and is developed upon the face, breast, and back, without constitutional disturbance.

Of the various salts of iron, the iodide is the only one commonly credited with the power of producing well-marked irritative effects upon the skin. The eruptions which may follow the ingestion of iodide of iron have been described as "erythematous," "papular or urticarial," "eczematous," and "pustular" in character. Since these irritant effects are most probably due to the iodine contained in the preparation, they will more properly be considered under the head of eruptions produced by iodine and its compounds.

### HYDRARGYRUM—MERCURY.

The application of mercury to the skin, as in the form of unguentum hydrargyri, occasions, as is well known, various degrees of irritation. The grade and extent of the inflammatory action will depend upon the strength of the preparation used and the duration of its contact. This may vary from a slight erythema to a high degree of dermatitis, and the formation of sloughs. The most common form is an erythematous or vesicular eruption. The vesicles

### GUARANA.

I have a note that Mantegazza described urticaria following the use of Guarana.

### GUIACUM.

Murrell records an eruption covering the arms and legs, accompanied by intense itching, in a man taking two drachms of confection three times daily. The confection was composed of 10 grains of guaiac resin to a drachm of honey. I saw this eruption, and it was a miliary erythematous eruption, closely resembling the ordinary copaiba rash.

### GURGUN OIL.

Montgomery, when gurgun oil was introduced by Sir William O'Shaughnessy in 1838 as a substitute for copaiba in gleet, recorded a case of eruption produced by it, resembling copaiba rash. I have no further record of this reference.—T. C. F.

are usually small, closely aggregated, and frequently develop into pustules, especially when seated around the hair-follicles.

The local application of corrosive sublimate in the form of antiseptic dressings, which is practised by so many surgeons at the present day, has been followed by eruptive disturbances in a large number of cases. Dr. Reichel reports the following case :—After an operation for genu valgum, the leg, from foot to pubes, was enveloped in the sublimate gauze. On the fifth day sensations of burning and itching were felt in the limb. Upon removal of the bandages the leg was found to be covered with an intense papulo-vesicular eczema ; the integument was œdematous. A general erythema was now developed ; the whole body, except face and neck, was thickly covered with small red spots, especially upon the breast, abdomen, scrotum, and back of elbows. Four days after the removal of the sublimate bandage the eruption disappeared. Numerous other cases of eczema mercuriale have been reported from the use of the sublimate dressing. Netzel reports a case of erythematous eruption about the pelvis, and extending over the body, resulting from the use of sublimate injections after confinement. Lessona observed at the Maternity Hospital at Turin three cases in which a peculiar roseolous rash followed the use of sublimate injections after childbirth. The rash first appeared upon the breasts, and was preceded or followed by salivation.[1]

The fact that eruptive disturbances sometimes follow the ingestion of mercurial preparations was recognised by Benjamin Bell, 1796, who first described eczema mercuriale. In a monograph published in 1804, Alley grouped under the general term Hydrargyria[2] several forms of eruption, which he described as H. mitis, H. febrilis, and H. maligna.

1. *Hydrargyria mitis.*—The eruption consists of a slight

[1] See also Brun's Thesis for other cases of this nature. Numerous instances of fatal poisoning from such injections were collected by Butte ('Nouvelles Archives d'Obstetrique et de Gynécologie,' 1886, and 'Med. Record, N. Y.,' July 10th, 1886). The occurrence of a rash is, however, exceptional.

Dubreuilh records a case of eruption following a calomel enema.—T. C. F.

[2] Morel-Lavallée suggests the retention of the term hydrargyrie cutanée to denote the effects on the skin, and the term mercurialismus to designate "l'ensemble des accidents dus à l'imprégnation mercurielle." These so-called

efflorescence localised in certain regions, such as the internal surface of the thighs, scrotum, the groin, and the lower segment of the abdomen, sometimes, but rarely, on the arms, back, and face. A close examination of these reddish patches reveals a multitude of minute vesicles filled with a transparent fluid. It is attended with intense itching, but the eruption usually subsides soon after the cessation of the medicine.

2. *Hydrargyria febrilis.*—This form may develop *ab initio*, or, as is more frequent, it succeeds the benign form, and manifests itself as a more severe inflammation of the skin. There is an intense scarlatiniform redness occupying the entire surface. Upon this appear, towards the fourth day, larger and more voluminous vesicles, coppery in tint, distended with a purulent fluid. These vesicles rupture and crust over, resembling the crusts of eczema. There is considerable fever and constitutional disturbance. Desquamation occurs in flakes, as in scarlet fever. Sometimes several successive exfoliations take place.

3. *Hydrargyria maligna.*—The phenomena of this stage are simply an aggravation or intensification of the preceding from a continuance of the drug after the vesicular eruption has declared itself. The skin becomes of a purplish-red hue, swollen and painful, and is covered with confluent vesicles or large bullæ filled with a sero-purulent fluid. The constitutional disturbance is correspondingly increased with the aggravation of the cutaneous symptoms ; desquamation takes place from the fourth to the eighth day, the epidermis peeling off in large flakes.

Small doses of the drug are capable of exciting an irritant action upon the cutaneous system. Alley saw it in one case after taking two grains of calomel, and in another case after three grains of calomel. Fournier, cited by Hallopeau, observed an eruption identical with that of scarlatina, which appeared on the face, trunk, and extremities of a patient who had taken five centigrammes of protiodide of mercury. It was followed by a desquamation even more

"mercurial eruptions" have also been named "mercurial erythema" by Edinburgh physicians, "mercurial eczema" by John Pearson, "mercurial lepra" by Moriarty, and "mecurial exanthem" by J. Frank.—T. C. F.

abundant than is observed after ordinary scarlatina. The same scarlatiniform eruption, followed by abundant desquamation, occurred after the use of acid nitrate of mercury and Dupuytren's pills.

Englemann reports a case of desquamative erythema after taking three doses, two and one-half grains each, of calomel. The eruption first appeared on the head, with œdema of the face, and in one night spread over the whole body; the patient had had similar experiences after taking mercurial pills, and also after having been exposed to mercurial vapors.

Blanchon reports the case of a woman exposed to fumes of mercurial vapour. After five or six days, a roseolar eruption first appeared on face and neck, and became generalised. On certain parts, as arms and upper part of trunk, there were figured and crescentic patches on a slightly reddened base, as seen in mobilliform erythemas. The eruption, which was not attended with constitutional disturbance, disappeared in five or six days.

Almost every form of eruptive disturbance has been recorded as occurring from the internal administration of mercury; urticaria, herpes, impetigo, purpura, furuncles, with ulcerative lesions involving considerable loss of tissue.[1]

[1] Järusoff reports a typical urticaria invariably following hypodermic injections of corrosive sublimate. The distribution of the eruption varied considerably in extent and localisation. Petersen records a generalised erythematous eruption, occurring half an hour after a calomel hypodermic injection. After a second injection a limited erythema was seen round the site of the prick. After a third injection nothing happened. In another patient a similar series of phenomena followed the injection of yellow oxide of mercury. Bürtzeff records a case in which a single friction of grey mercurial ointment was rapidly followed by an eruption of papular erythema all over the body. A rash also ensued after a hypodermic injection in the same patient, and after the ingestion of a single dose of mercury. Kaposi saw an erythema multiforme follow mercurial friction, and Steinberg attributed a generalised erythema to the local action of Emplastrum de Vigo. Moriflier mentions a generalised bullous eruption following frictions of a mercurial belladonna ointment to the scrotum. See also the bullous eruption described by Petrini.

Morel-Lavallée has recently discussed the subject in an interesting and elaborate paper. The occurrence of these eruptions was almost forgotten and even denied, but more recent observations have conclusively established that a "hydrargyrie" of internal, or, to use Bazin's term, of pathogenetic, causation undoubtedly can occur, similar in type to the eruption produced

*Tests for Mercury.*

The most certain method of detecting mercury in the urine is by electrolysis, that is, by causing it to be deposited, in a metallic state, upon either gold or copper (or certain other metals), and then examining the deposit for its identity.

Take a piece of bright gold wire (or some other smooth

by the external application of mercurials. He points out that these eruptions have recurred in the same patient with the repeated administration of mercury, either in the same or a varied preparation, and have followed, not only the internal exhibition of the drug, but also the external application of Neapolitan ointment, sublimate dressings, and the acid nitrate, vagino-uterine injections of the sublimate or biniodide, a calomel enema, and the inhalation of fumes. Gaucherant recognized three forms of eruption, viz., the scarlatiniform, the usual type; the eczematous, described by Alley; and other rare forms (rubeoliform, urticate, &c.). Morel-Lavallée considers a classification founded on the elementary lesions to be antiquated, and thinks that, if any grouping of the cases be called for, it would be better to have regard to the gravity and duration of the disturbance, and to note a *discrete, fugacious and insignificant form* (H. mitis), *an intense form*, and a *grave or even malignant form* (H. maligna). He does not accept Alley's second class "*simplex febrilis*" because amongst those cases which can be regarded as *mites*, judged by their duration and reaction upon the economy, a great number have commenced by general symptoms and a febrile malaise, at least in the invasion period, and, on the other hand, in more severe cases febrile movement has been slight or absent. The habitual type of the eruption is scarlatiniform, but, as far as our limited knowledge of the effects of intoxication by vagino-uterine injections goes, such eruptions incline rather to take on the polymorphic aspect of a macular, papular, or urticated roseola. Morel-Lavallée gives the following analysis of the twenty-two cases collected by him. The hydrargyrie succeeded the ingestion of the first dose at the following intervals of time: after several weeks, four times; after some days, five times; from a day to several hours, nine times. In most cases only a single dose was given. The existence of *prodromata* is the rule. They are almost nothing in the slight cases, where the itching and burning dryness of the teguments precede by very little the eruption, which, however, at times, when it is very discrete, shows itself at once. It is usual to see them inaugurate the affection with a suddenness and intensity sufficient to stimulate fever. It is a sudden illness, with violent fever, insomnia, cephalalgia, dryness of mouth and pharynx, anorexia, and general aching or a shiver. These symptoms subside, as a rule, on the appearance of the eruption, except in grave cases. In one case there was photophobia; in one, loss of voice. The *eruption* commences in different ways, most often by plaques of various dimensions, not prominent, with sinuous contours, dis-

article of gold), wind about it, in a spiral form, a piece of bright iron wire, and immerse the whole into the urine, slightly acidulated with hydrochloric acid. Any mercury present will be deposited partly on the gold, partly on the iron.

Or, dip into the acidulated urine a piece of bright copper-foil, with a piece of zinc-wire wound about the upper

appearing momentarily on pressure, more marked on the abdomino-femoral regions, where they begin to coalesce. On the rest of the trunk there may be other less numerous and indistinct plaques. At other times there may be seen a diffuse scarlatinoid eruption, in large sheets of an uniform colour, but diffusing gradually to the periphery, where the redness becomes granulated. Sometimes it commences on the limbs, and then either it is a diffuse granular redness without distinct limits, or else, on the contrary, the eruption begins by rosy morbilliform tâches, which may become urticated, then papular, and finally coalescent. The commencement on the face has been once noticed. Itching is often most intense. The inguino-pubic region is most contantly and extensively affected. The scalp escapes. In a more severe degree the erythema is more persistent and generalised. The eruption may become vesicular and pustular; vesicles are only seen, as a rule, in the axillary and inguinal regions, and in the localised discrete erythematous eruptions due to the inunction of grey ointment. In the grave cases, oozing over considerable areas and true phlyctenæ are sometimes seen. The œdema may be considerable. Desquamation is often very marked and persistent in severe cases.

*Primary General and Visceral Symptoms* due to the mercurial intoxication, must be distinguished from secondary disturbances due to the extensive affection of the skin. Stomatitis, or, at least, gingivitis, is frequent. There may be diarrhœa and vomiting, and prostration. Insomnia and delirium may occur in grave cases.

The *Duration* may be ephemeral or extend to six months. The average is eight to twenty days. The *Prognosis* may be serious, especially if the etiology be not recognised. The *Diagnosis* is frequently very difficult, unless the practitioner be experienced in such matters and on the alert. Not to mention measles, the initiatory variolous rashes, and divers medicinal eruptions, it will be sufficient to point out specially scarlatina, primitive exfoliating dermatitis, eczema rubrum, and erysipelas.

As to *Etiology*, individual susceptibility has a powerful influence, and it is to be noted that two of the cases were affected also by terebinthinates and chloral. In ten of the twenty-two cases the eruption returned when mercury was again exhibited, and even when different preparations were used. Leaving aside external inunctions, calomel is the most frequent cause, but the eruption has followed the use of Van Swieten's liquor, Vigo's plaster, the proto-iodide, sublimate pills, mercurial pills, the application of acid nitrate of mercury, sublimate baths and dressings, a calomel enema, and vagino-uterine injections of the sublimate or biniodide. It has occurred after a single dose of calomel.—T. C. F.

part. In this case the mercury will be deposited on the copper.

The next step is to identify the deposit as mercury. For this purpose, introduce the amalgamated metal into a glass tube closed at one end, and heat it. The mercury will become volatilised and be deposited in the cool part of the tube. The deposit may be distinguished from the similar one produced by arsenic and antimony by its not being oxidised to white compounds (oxides) when it is heated with access of air, and further by the fact that it is not rendered yellow or orange by hydrosulphuric acid, but black, which colour is, however, only superficial. Sulphide of ammonium converts it completely into black sulphide of mercury.

## HYOSCYAMUS.

Although the physiological action of hyoscyamus so closely resembles that of belladonna and stramonium, yet its irritant action upon the skin is less strongly pronounced than that of the two other drugs, and the eruption is less vivid in colour.

The most common form of eruption produced by the internal use of hyoscyamus is erythematous. The congestion of the skin is usually preceded by burning and itching, and attended with more or less œdema, sometimes with the production of urticarial wheals.

White describes a case in which there were burning and pricking sensations in the hands, feet, and legs, and a generalised purplish rash, especially upon the face and neck, with great swelling of the parts. Craik reports the occurrence of a red rash-like scarlatinal eruption in a child, caused by eating the leaves of the hyoscyamus.

Bessières reports a case in which the patient was accustomed to use vaginal injections of a decoction of hyoscyamus, but suffered from an erythematous eruption after the same injection *per rectum*.

Pustular as well as purpuric eruptions have several times been observed from the repeated internal use of small doses of henbane.[1]

[1] Cabot (quoted by G. H. Fox) describes the face and body as becoming

### IODINE—IODIDE OF POTASSIUM—IODIDE OF AMMONIUM—IODIDE OF SODIUM, ETC.

The iodic eruptions include all changes in the skin caused by the alkaline iodine salts. All of the various compounds of iodine are capable of producing disorders of the cutaneous system; but, since the drug is usually administered in the form of iodide of potassium, the eruptions recorded under this head may be regarded as representative of the whole class. The eruptive disturbances connected with the use of iodoform will be considered separately.

The local action of iodine, either in the form of the tincture or vapour upon the healthy human skin, is well known. The skin is first stained yellow and then assumes a brownish-red colour. The epidermis is shrivelled and loosened from its attachment, and desquamates in flakes. This process is attended with burning, itching, and more or less pain. The effects are not limited to the point of application, but may be manifest on different parts of the body in the shape of papular, pustular, or even bullous eruptions. These irritative effects upon remote portions of the body are most frequently observed after repeated applications of the tincture and are probably consecutive to absorption of the drug. It has been observed that erythematous patches have appeared upon the body after the injection of an ovarian cyst with tincture of iodine. Similar effects have followed the injection of the tunica vaginalis after tapping for hydrocele. Simon and Regnard observed, after the application of tincture of iodine with glycerine to the erythematous scalps of children, an extensive papular eruption on the face and other parts of the body.[1]

red, hard, and shining after the administration of hyoscyamus. There were no typical wheals, but the patient could hardly speak from stiffness of the tongue and lips. The eruption subsided shortly after the third hourly dose was given.

Robert Lawson, in a report on the use of *hyoscyamine* in some mental maladies, says it only rarely causes an exanthem.—T. C. F.

[1] Polotebnoff observed a case of generalised erythema papulatum following friction with Tinct. Iodi. At a subsequent stage a local reaction only followed the application. Locquin recorded a symmetrical erythema

The occurrence of cutaneous disturbances from the ingestion of iodide of potassium have been recognised since its introduction into the materia medica, although certain rare and somewhat singular effects upon the skin have not been recorded until within a few years past.

The literature of iodic eruptions, comprising almost innumerable observation relating to all forms of cutaneous disorders, from simple erythema to the severest forms of dermatitis, attended with severe constitutional reaction, is so vast that its mere enumeration would require several pages.

Fischer, who, as early as 1859, made a special study of iodic eruptions, divides them into four principal forms, the erythematous, the urticarial, the nodulo-pustular, and the eczematous. Since then, with the widening of our knowledge of the range of pathogenetic action of this drug, new eruptive elements have been recognised. Fournier, though by no means the first to describe the petechial form, has traced its clinical characters with precision. The bullous form, first described by O'Reilly, of New York, has been carefully studied by Bumstead and others.

Quite recently Celso Pellizari has reported two very rare cases, in which there were large inflammatory nodular masses, varying in size from that of a nut to the size of the fist, seated in the subcutaneous cellular tissue, accompanied by high fever, followed by abscesses which healed slowly and left cicatrices. Besnier has still more recently called attention to a carbuncular eruption, under the designation of eruption anthracoide iodo-potassique.

The iodic eruptions may be classed according to their elementary lesions, as follows :

*The erythematous form.*—This usually occurs on forearms, face, and anterior surface of the chest. The redness may be diffuse, or appear in discrete and irregular spots or in large circumscribed patches ; exceptionally it may extend over the whole surface of the body. This hyperæmia may be intensified and developed into—

*The papular and urticarial form.*—There may appear upon

of the hands following the application of Tinct. Iodi to one of them.—T. C. F.

reddish patches, or upon the skin uniformly congested, intensely red, slightly-raised papules, which are frequently grouped. In some cases, the larger papules are surrounded by an areola. The eruption is principally developed upon the hypogastrium and the extremities, but may be general. The papules have a certain analogy with an ordinary urticaria, from which they differ by their exaggerated development, there brighter colouration, generally described as rose red, and which becomes pale on pressure. Besides the difference of colour, there is sometimes seen, as in a case of Pellizari's, a kind of telangiectasic condition suggesting nævus maternus.

Pellizari has more recently presented a report of several cases of iodic eruption, in which the characteristic features were those of urticaria and papular erythema. In one case the urticarial nodules became converted into phlyctenulæ, containing sanguinolent pus. Large ecthymatous pustules, anthracoid acne, nodules of variable form, and numerous superficial abscesses were also present, constituting a polymorphous eruption.

Taylor recently brought before the New York Dermatological Society a patient, in whom an urticarial eruption had been developed twice by a few fifteen-grain doses of the iodide of potassium. The eruption was confined to the face, neck, backs of hands, and wrists. Many of the wheals were surrounded, on the second day of the eruption, by pellucid vesicles.

*The vesicular form* may also develop from the erythematous. Berenguier describes a scarlatiniform rash of sudden occurrence upon the chest and limbs, upon the surface of which were numerous small, discrete vesicles. Mercier reports a case of an iodic eruption resembling eczema rubrum, accompanied with severe fever, and characterised by an extremely copious exudation of fluid. The same eruption was reproduced in the same individual in both instances by moderate doses. An eczematous form, which is said to be very rare, develops especially on the hairy scalp, and in the neighbourhood of the scrotum.[1]

[1] Leloir has seen an eruption, due to iodide of potassium, simulating "the itch" to the life, both by its localisation and accompanying pruritus.

*The bullous form.*—Comparatively few cases of bullous eruption caused by the ingestion of iodide of potassium are found recorded in the literature of drug eruptions, and it may, therefore, be classed among the rarer cutaneous manifestations of the drug. A most remarkable case of this eruptive form recently came under my observation at Charity Hospital.

The patient, Albert S—, a German, about fifty years of age, had been taking a solution of iodide of potassium (1 in 2), ʒj, t. i. d. Three or four days after beginning the use of the medicine there was observed an erythematous condition of the face, with the production of vesico-pustules about the size of a pea. Under the continued influence of the drug, the dermatitis increased in intensity and severity, and the vesicles developed into bullæ of varying size. The iodide was discontinued after ten days treatment, when he had taken nine hundred grains altogether. He was then given sulphide of calcicum, one-fifth grain three times a day for three days, when he was transferred to the Dermatological Ward, October 9th, 1885. Upon admission the entire face, the ears, and the neck down to the level of the hyoid bone was found to be the seat of an eruption, also the dorsal surfaces of hands and wrists. The integument of the forehead and face was bright-red, and infiltrated to such a degree as to be a quarter of an inch thicker than normal, causing the natural lines of the skin to appear like deep furrows. The skin appeared as if thrown up into prominent bosses or ridges, separated by intervening depressions. The enormous tumefaction of the supra-orbital folds gave a leonine appearance to the face. The eyes were closed from the œdematous condition of the upper and lower lids.

The face, and especially the forehead, was thickly studded with small vesico-pustules, many of which had broken, leaving a mass of crusts. Upon the upper portion of the forehead, the fusion of the closely-crowded bullæ had formed a belt or zone of raised epidermis, simulating in appearance the advancing border of an erysipelatous inflammation, which

Duhring records a case in which Tilbury Fox's dysidrosis was exactly simulated.—T. C. F.

stopped abruptly at the line where the hair began. The dermatitis, both of the face and posterior portion of the neck, did not encroach upon the hairy scalp. The swollen alæ of the nose were covered with a number of pea-sized lesions, some of which had become pustular. The ears were greatly swollen, and where the crusts from ruptured bullæ had been picked off by the patient, bloody crusts were to be seen. The skin became pale on pressure, but did not pit, and immediately resumed its red colour when the finger was withdrawn.

Upon the dorsal surface of the hands and wrists, the skin was reddened and infiltrated, though not to the same degree as upon the face. On the dorsum of the left hand, from the wrists to the tips of the fingers, were a number of bullæ varying in size from a three-cent piece to that of a silver dollar.

Upon the right forearm, above the wrist, there was one large bulla and two smaller ones, with a few vesico-pustules. The back of this hand was occupied by a large bulla, the size of a pigeon's egg, surrounded by a number of smaller ones, suggesting in their arrangement a magnified herpes iris; toward the ulnar or outer border were four or five bullæ, ranging in size from a large pea to that of a cherry; the second, third, and little fingers were occupied by bullæ extending along their entire length to the tips, the walls tensely distended with a sero-sanguinolent secretion. Both hands presented a swollen, puffy appearance. There was no eruption upon any other portion of the body. Examination of the mouth and fauces revealed nothing beyond an intense congestion of the mucous membrane. The patient was in a state of profound prostration; he was dull and stupid, and could be aroused with difficulty; there was more or less tremor of the hands, and he was constantly moving them toward his face. His respiration was quickened and his pulse was 120, temperature not taken.

October 10th.—The general appearance of the face was about the same as yesterday. The bullæ upon one hand had become coherent at their bases, but did not coalesce. Upon the other hand the lesions had become confluent, forming an enormous bleb, extending from the annular ligament of the

wrist to the tips of the fingers. The colour was a steely blue, bearing a striking resemblance to the appearance of a coil of intestine. The general condition of the patient unchanged; resp. 23, pulse 112. Catheter will not pass on account of stricture at four and a half inches, admitting No. 10 sound with difficulty. Urine duct kept in bed with patient. He was placed upon an extra diet, and ordered whisky, ℥iv per diem, the face and hands to be dressed with carbolised vaseline. Some of the bullæ were punctured, yielding a reddish serum, which was examined for iodine with negative results.

11th.—No change in appearance, except that some of the older bullæ on hands have become dirty-blue in colour, and on puncture give exit to a dirty-red sero-pus instead of a clear serum as before. Examination of heart showed a systolic apex murmur transmitted towards left axilla. Diagnosis of mitral insufficiency. Temperature, 100·1°; resp., 22; pulse, 114.

12th.—Infiltration of the skin has subsided somewhat: examination of the urine shows it acid in reaction, sp. gr. 1·010, with a considerable amount of albumin, 10 to 15 per cent. Under the microscope a few pus and blood globules are seen; no casts.

14th.—On the back of the neck the skin has returned to its normal level, but is still red, the face less swollen, eyes well open and bright in appearance, leonine appearance of countenance gone. The bullæ on hand present a blue-black coloration. A bloody pus, slightly offensive, comes from one or two ruptured bullæ. All the bullæ were ordered to be cut open, washed out with 2½ per cent. carbolic solution, and dressed with carbolised vaseline. The floor of some of the bullæ is bathed in pus, apparently due to superficial ulceration.

21st.—Continued improvement in general condition of patient; the backs of the hands cleared of and presenting a healthy appearance.

29th.—The skin of the neck and a good part of the face has returned to its normal condition, though still somewhat hyperæmic. Raw surfaces on dorsum of hands and fingers healing.

November 5th.—Almost all traces of the eruption gone, though no gain in the patient's general condition. Patient has cough. Examination of chest shows dullness at apices of both lungs, with increased fremitus, prolonged high respiratory murmur, and few moist râles. Passes urine and fæces in bed as on entrance.

15th.—Patient has continued to fail. Increasing frequency and feebleness of pulse (120); resp. 32. Examination of chest shows pulmonary œdema.

16th.—Patient died quietly at 2 p.m.

Autopsy showed *heart* enlarged and dilated on left side. Insufficiency of mitral valve and atheromatous deposits. Aorta atheromatous. *Lungs* œdematous; phthisical consolidation at both apices; no cavities. *Kidneys* somewhat diminished in size and heightened in colour; consistence increased; surface granular; capsule adherent. *Liver* and *spleen* normal.

The drawing representing the face in the picture (*vide* Frontispiece) was made on the second day after the admission of the patient, when the more acute eruptive features had begun to subside. The direct dependence of the eruption upon the iodide of potassium in this case would seem to be conclusively established; first, by the appearance of the cutaneous phenomena within three or four days after commencing the use of the drug; second, by the intensification of all the eruptive features under its continued use; third, by the subsidence of the eruption soon after the drug was withdrawn, and, fourth negatively, by the absence of any other known exciting cause.

In this case the eruption did not attain its maximum development until four or five days after the iodide was discontinued. Whether the sulphide of calcium, given in the interim, exerted any material influence in intensifying and perpetuating the eruptive tendency, is open to question.

The comparatively slow involution of the lesions was probably due to the profound systemic depression caused by the drug, and the existence of the grave organic troubles, which ultimately proved fatal.

As early as 1842 Ricord refers to a rupia-like eruption, presenting the characters of a cachectic rupia, which he had

observed upon the forearms and legs of a patient who was taking iodide of potassium. The eruption disappeared upon discontinuing the drug, and reappeared when its use was resumed. While this eruption was probably closely allied, if not identical, with that under consideration, its clinical characters were not traced with sufficient precision to justify its inclusion under this category. The first authentic case of bullous eruption caused by iodide of potassium was reported by Dr. John O'Reilly in the 'New York Medical Gazette,' January, 1854.[1]

The special features which characterise this eruption are the development of bullæ of varying size, often commingled with vesicles and small pustules. The lesions usually make their appearance as vesicles or vesico-pustules, which rapidly increase in size, forming regular rounded or globular bullæ, from the size of a pea to that of a pigeon's egg, or even larger; they may remain discrete, or coalesce with neighbouring bullæ; in which case they may attain enormous dimensions. In other cases they begin as hard papules, the shot-like character of the papules suggesting the commencing stage of variola. This resemblance is heightened by the rapid transformation of the papules into vesicles, and their tendency to umbilication, which is quite manifest in some cases. There is generally more or less thickening or infiltration of the skin, and the lesions may be surrounded by an inflammatory areola, variously described as "erythematous," "bright-red," or "a dark wine colour" In some cases the epidermis is uplifted without inflammatory swelling of the skin, presenting the appearance of a blister produced by a burn. In one case the eruption was described as "an eruption of blisters, compared to "potato apples," each blister surrounded by a series of bright-red concentric rings.[2]

[1] Sloughing occurred in the sites of bullæ, and the penis was lost. Crocker refers to a case in which a case of "hydroa" was aggravated into a gangrenous condition by the use of iodide of potassium.—T. C. F.

[2] Hallopeau in 1888 recorded a remarkable case in which a similar eruption and intoxication effects recurred seven times in a man suffering from phthisis and albuminuria. Bullæ were produced on the face, forearms, and lingual and palpebral mucous membranes. The bullæ had citrin or purulent thickish contents. If the drug was continued new bullæ evolved, inflammatory effects increased in the old ones, and led to crusting, atrophy of

In a number of the cases there was a coexistence of renal and cardiac complications which may explain the comparatively large fatality observed. We can readily understand why defective elimination of the drug should act as a co-factor in the causation of cutaneous irritation. The greater part of the iodine is normally eliminated by the kidneys within twenty-four hours after its ingestion; when this channel of egress is blocked up, the drug is longer retained in the vascular channels, and exerts its irritant action upon the tissues. But why cardiac disorders should produce a morbid determination of the drug's action towards the cutaneous system is not so evident. Thin has suggested that this may be due to the feeble heart impulse and consequent sluggish circulation in the cutaneous capillaries, allowing the iodine, or its compounds present in the blood, time to attack and injure parts of the vascular wall. It is needless to say that the retarded elimination of the drug does not explain the occasional occurrence of the eruption within a few hours after the ingestion of a single insignificant dose.

*The papulo-pustular form.*—This may be regarded as typical, as it is the most common, of the eruptions provoked by the action of the iodides. It presents certain analogies with the acneiform eruption produced by the bromides. It usually appears upon the face, backs of shoulders, upper part of chest and arms, where the sebaceous glands are

the derma, condylomatous vegetations, and remarkable cicatricial bridles. The diagnosis was obscure for a time, and tertiary syphilis and pemphigus vegetans had to be eliminated.

Taylor has met with three instances of the bullous eruption, in which after rupture of the lesions, surfaces varying in appearance between the slightly warty and the vegetating were left. He states that all cases of bullous iodic eruption shew a condition of inflammatory thickening of the skin in marked contrast to pemphigus. This statement is, however, too absolute. Hyde has insisted on the point that in addition to a polymorphic eruption two types of bullous or quasi-bullous eruption are met with, viz. the bullous type, pure and simple, and a type of quasi-bulla or molluscoid formation, with solid bases and thick or almost solid contents, not developing like true bullæ and never attaining that form. Compare on this subject Morrow's, the Sydenham Society's, and Tilbury Fox's plates. The truth is, I believe, that these two types are connected by a complete chain of links.

The lingual and buccal mucous membranes may be involved.—T. C. F.

abundant. Sometimes, however, it surpasses these limits, and is found distributed over a large surface of the body. The eruption commences as hard shotty papules, which usually enlarge and become surmounted by small pustules, when fully developed. The iodic pustules may be described as consisting of acuminated or rounded eminences, more or less voluminous, with a reddened, somewhat infiltrated base, suppurating sometimes only at the summit, at other times in the totality of the pustule. The contents of the pustule concrete into a yellowish crust, which may persist for some time, and on falling leave a distinct cicatrix. Sometimes the tubercles, instead of ulcerating, become transformed into nodules of firmer consistence, intensely red, deeply seated in the tissues, which are remarkably slow in their involution.[1]

*The anthracoid form.*—In this connection may be described an eruption of carbuncular lesions which resembles the "confluent acne" produced by the bromides. Besnier designates it as *acné anthracoide iodo-potassique.* In his two cases the face and thorax were covered with veritable tumours of variable volume, of a reddish coppery hue, flabby, almost fungous, and presenting punctate depressions or vacuoles analogous to those of anthracoid furuncle. It was impossible to express their contents; incision gave exit only to blood. In Duhring's case there was a confluence of the nodules, forming a sharply-defined, rounded, inflammatory patch, violaceous in colour, its centre depressed and crusted, while the periphery was studded with numerous deep-seated, yellowish, sebaceous-looking pustules, presenting an acneiform appearance. When cut into, the yellowish

[1] It is to be noted also that the papules may vesiculate and pass into the bullous form of eruption. The amount of inflammatory base present, the depth to which the skin is involved, the intensity of the process, the size of the lesions, and degrees of confluence vary widely in different cases and even in the same case. From these papulo-vesicular and papulo-pustular lesions, often resembling acne, varicella, and variola, may arise the ecthymatous, bullous, molluscoid, condylomata-like, and other forms of eruption.

In infants the eruption may closely simulate the bromide eruption both in aspect and site. Koplik, it may be well to mention, has observed an iodic eruption in an infant nursed by a mother taking iodide of potassium. —T. C. F.

pustular points bled, but did not exude their contents. When the crust was lifted from the central lesion, it showed a red, glistening, firmly-mammillated or warty surface. There were four of these lesions occupying the forehead, cheeks, and nose. The one on the forehead was two inches in diameter. In a case of Dr. Costa's, referred to by Atkinson, the lesions were situated upon the back and chest, as well as the face. The suppression of the medicine was followed in all of these cases by the involution of the lesions in about two weeks, some of them leaving a brownish macule, with cicatricial depression.[1]

*The petechial form.*—Although Ricord, as early as 1842, mentioned among the eruptions produced by the iodide of potassium the occurrence of "petechiæ resembling the spots of the morbus maculosus Werlhofii—a veritable purpura hemorrhagica"—Fournier was the first to carefully study the purpuric eruption. He describes the lesions as discrete, miliary, millet-seed to lentil-sized spots, usually rounded, more rarely oval or discoid in form. Its seat of predilection is the legs, more especially the middle three-fifths, avoiding the knees and feet, and developed more profusely on the anterior than the posterior surfaces. Ordinarily there are as many as one hundred discrete spots on each leg. Petitjean describes a case in which the eruption appeared on the dorsal surface of the feet, and another observer saw it upon the forearms and wrists.

According to Fournier, the explosion of the petechial accidents almost invariably occurs soon after the commencement of the treatment, usually in from one to three days.

[1] R. W. Taylor, in recording a case of the so-called *Acné anthracoïde iodo-potassique* under the name *Dermatitis tuberosa*, holds the view that the essential lesion in all forms of iodide eruption, except the purpuric, is a dermatitis, and that they only differ in non-essentials of form, degree of development, modification, and transformation. In the particular phase under consideration there is added to the dermatitis a peculiar involvement of the sebaceous glands, evidenced by the exuding cribriform openings and pus crusts. The tumours may develop into sessile and mushroom forms, simulating mycosis fungoides, and present a papillary hypertrophy of various degrees of intensity. Papules, papulo-pustules, tubercles, tuberculo-pustules, diffuse inflammatory patches often fungating, and subcutaneous nodular inflammation may co-exist, and are all phases of dermatitis with secondary modifications.—T. C. F.

The eruption reaches its height in two or three days, and, if the medicine be discontinued, disappears in the course of two or three weeks. In certain persons the same eruption may occur several times after each new use of the iodide.[1] In the course of a continuous treatment, each notable elevation of the dose was followed by a marked recrudescence of a new crop of purpura ("*une poussée subintrante*"), contrasted by their vivid colouration with the faded earlier eruption.

Fournier regards the eruption as rare, as he had observed it only in fifteen cases. I have seen several cases. In one old lady, I redeveloped the eruption four different times, in order to test its causal connection with the iodine. She had been taking the medicine some time in small doses when my attention was called to the eruption. Each time thereafter it was reproduced within forty-eight hours by the use of five-grain doses of the iodide. S. Mackenzie reports a remarkable case of iodic purpura in a child, caused by a single dose of two and one half grains. The case terminated fatally.[2]

It has been suggested that iodic purpura is more apt to occur in anæmic, debilitated persons who have taken the drug for some time. This view has not been confirmed by my own experience, nor that of many others. Fournier emphasises the statement that an anæmic condition or syphilitic cachexia could not be regarded as a predisposing cause. Two thirds of his patients were absolutely exempt from every manifestation of syphilis at the time when the iodide, given as a preventive of further accidents, determined the eruption.

*Nodular form.*—Vallanur reports a case in which a woman, after taking two and one half grams of the iodide for four days, was attacked with acute pains in the but-

[1] Besnier holds that pure iodine will not cause the hæmorrhages, and he illustrated this fact in the person of a man who had purpura on the lower limbs every time he took iodide of potassium, but though tincture of iodine caused symptoms of iodism there was no purpura produced.—T. C. F.

[2] A portrait is given of the head of the child in the 'Illustrated Medical News,' November 17th, 1888. See also the fatal case of pemphigoid eruption and Purpura hæmorrhagica reported by Elsner; also Wilson's case. —T. C. F.

tocks, thighs, calf of the leg, and dorsal region; then there appeared upon the painful points small indurated nodules of the size of a nut, of a deep red colour. During three days they increased in size, one or two attaining the size of an egg. The iodide was discontinued, and the nodosities rapidly disappeared. Some days later the iodide was again administered, and the same cutaneous accidents were reproduced. This experiment was repeated three times, always giving the same results.

Talamon reports the case of a woman in whom two and one half grams of iodide of potassium produced an eruption resembling erythema nodosum. There were at least twenty red and indurated nodules situated upon the lower limbs, the loins, and buttocks. The lesions were made to reappear at three different times by the use of the iodide.

Hallopeau observed the development of painful nodes in one of his patients, which was repeated every time he took the iodide of potassium. The tumours were oval in shape, reddish at the surface, and painful on pressure; they were situated chiefly on the anterior surface of the thighs. In conjunction with the nodular eruption the patient also had iodic purpura.[1]

*Polymorphous eruptions.*—While the particular form in which the iodic eruption is manifested in different persons is, as a rule, unique, and determined principally by the constitutional reaction of the individual, yet it sometimes happens that a combination or association of different eruptive elements is met with in the same individual; we have seen above that papules, tubercles, and pustules may co-exist in the papulo-pustular form, the papule representing the first stage of the morbid process, of which the pustule is the acme or completion. Ecthymatous pustules and furuncles may begin as hard papules, nodules may suppurate and

[1] Hallopeau points out how these subdermic nodosities may simulate gummata or rheumatismal nodules. See also the cases reported by Ricord, Pellizari, Morrow, and Hutchinson. Kaempfer noted similar cutaneous infiltrations on the legs, recurring with increased violence and profound intoxication each time the drug was resumed, so that some of the infiltrations attained the size of the palm of the hand. The eruption reappeared after the administration of the drug in very small doses *per rectum*.—T. C. F.

follow all the evolutions of a subcutaneous abscess, the successive stages representing different forms of lesions.

I recently presented a case before the New York Dermatological Society in which ten-grain doses of iodide of potassium developed a polymorphous eruption, preceded by intense lachrymation, coryza, and œdema of the face and eyes. The whole of the nose presented on the third day of the eruption a red, fungoid appearance, being greatly enlarged. The forehead, face, neck, and forearms were also the seat of the eruption. On the left cheek was seen a furuncle; over the malar bone a large, dark bulla; on the forehead were many papules and pustules. The eruption on the back of the neck very much resembled molluscum contagiosum. On the forearms there was a variety of eruptive elements—papules, tubercles, vesicles, pustules, and bullæ.

In a case reported by Celso Pellizari, three eruptive forms of an entirely different character were present at the same time, viz. on the left forearm, near the wrist, there were three slightly elevated papules, the size of a cent, with a rough surface and a dark strawberry colour. Upon the arms and legs were eight or ten eruptive elements, about one half inch in diameter, similar to the bullæ of rupia, surrounded by a circumscribed dark-red areola; and on the top there was a bulla like that produced by a burn, altogether different in character from the cachectic or syphilitic form; the third form was represented by three tumours, from the size of a nut to that of a small apple, deeply seated in the subcutaneous tissue. On stopping the iodide the papules quickly disappeared; the bullæ dried up, leaving scars which soon became white; the nodules disappeared more or less quickly, according to their size. The eruption was redeveloped in this case several times by the renewal of the iodide, each time accompanied by a high temperature, &c.

The distinguishing characteristics of iodic eruptions are their multiformity, their frequent occurrence after small doses of the drug, their usual prompt disappearance after its use is suspended, their frequent association with its well-known physiological, as well as incidental abnormal effects upon other organs, their proneness to develop in connection

with cardiac and renal disorders. Though usually of transient duration and insignificant import, they may be attended with the gravest symptoms, and exceptionally may lead to a fatal termination.

The length of time which intervenes between the administration of the drug and the first appearance of the eruption varies according to the size of the dose and the predisposition of the individual; usually it is from the third to the sixth day. This period may be reduced to a few hours, or lengthened to several weeks; in general it may be said that, while it may require several days to develop the eruption the first time; after its disappearance a single small dose may suffice to redevelop it in the course of three or four hours. A half-grain of iodide of potassium has been known to reproduce an urticarial eruption developed in the first instance by five-grain doses. In a case reported by Duffy, the patient had taken the iodide for over a month, thirty grains a day at first, afterwards sixty grains per day —two and one-half ounces in all—before the eruption appeared. It was redeveloped by forty-five grains in one day. Exceptionally the eruption may continue to come out after stoppage of the drug. In Besnier's case a bullous eruption was first developed by two grams, the second time by one gram, and the third time by ten centigrams. There seems to be no definite relation between the size of the dose and the form of the eruption; this would appear to be a matter of individual constitution. The acneiform eruptions have been more often observed after protracted use of the drug, while the bullous and petechial forms have shown themselves more promptly. The exceptions which have been noted to this rule, however, prove that the determination of the different varieties is independent of the mere fact of chronicity of treatment.

The cutaneous phenomena caused by the internal administration of iodide of potassium are undoubtedly due to the contained iodine, and *à priori* we should conclude that identical effects would follow the use of all the iodine compounds, especially the alkaline salts. It has been affirmed, however, that the different salts exert this irritative influence in different degrees of intensity, the iodide of ammonium

representing the highest degree of pathogenetic power, the iodide of potassium the next, and the iodide of sodium the least. It must be admitted that the observations upon which this comparative estimate is based are too few in number to justify conclusions possessing scientific value. In Duffy's case, iodide of sodium was given in ten-grain doses three times a day for eight days, with failure to reproduce an eruption of "iodic purpura" which had previously been twice developed by iodide of potassium. Iodide of ammonium being then substituted, two doses, twenty grains, brought out the eruption within twelve hours. In a case reported by Ringer, thirty grains of iodide of potassium for five days developed a pustular eruption, which disappeared within a few day after stoppage of the drug. The eruption was redeveloped by the same treatment, to again disappear when the medicine was discontinued. The iodide of ammonium was now ordered in ten-grain doses three times a day, and the eruption appeared after the second dose. The iodide of sodium was then substituted in the same doses, and continued for four days, but without bringing out the eruption, which, however, promptly reappeared after a single dose of iodide of ammonium.

*Pathogeny.*—The first requisite for a clear understanding of the pathogeny of iodic eruptions is the determination of the anatomical seat of the lesions. It was formerly believed that the sebaceous glands constituted the points of departure of all iodic eruptions, but it is hardly probable that eruptive elements so dissimilar as pustules, petechiæ, and bullæ, &c., should have a common starting-point.[1] Their very multiformity constitutes a fatal objection to such an assumption. It is well known that iodine, while principally eliminated by the kidneys, has been found in the saliva, sweat, and other physiological secretions. Adamkiewitz claims to have demonstrated its presence in the pustules of iodic acne, and therefore concluded that the sebaceous glands secrete iodide of potassium. He believes

[1] The congestive conditions in the face, &c., are common to many drugs, and with the urticaria and petechiæ possibly own a causation different from the various forms of dermatitis which are special to iodine and bromine. —T. C. F.

that the iodide undergoes a chemical modification by contact with the contents of the sebaceous glands, forming irritating compounds. Fox asserts that the iodic lesions are situated in the follicles, and are due to excessive stimulation of the sebaceous structure consequent upon elimination of the drug through this channel. The bullous form and other unusual and severe phases of the eruption he regards as exaggerated acneiform lesions, with excessive and altered secretion of sebum.

This view is opposed by other authorities, who go so far as to deny the existence even of iodic acne. Duckworth says that the glands are not the seat of pustular acne, and records a case in which the same eruptive form appeared in cicatricial tissue, where probably no glands remained. Other observers have noted its occurrence on the palms, where the presence of sebaceous glands has never been demonstrated. Thin, who rejects the theory that iodine eruptions are produced by stimulating effects on the secreting elements of the sebaceous glands, believes that all the varieties of the eruption may be explained by the tendency of iodine, when present in the blood current, to attack and disorganise the vessels at special points. "The injury in its mildest form is seen in common iodic acne, in more severe forms in the bullous and pustular eruptions, and in the worst form in iodic purpura. In the first we have limited œdema with congestion of the vessels; in the second, an effusion of serum, with more or less of the formed elements of the blood; in the third, destruction of the wall of the vessel and hæmorrhage." In the explanation of the severer forms he suggests that a sluggish circulation and deficient excretion may find a place.

In his microscopic examination of a bulla produced by iodine, he found that the lesion was formed by injury to the walls of the blood-vessels of a limited area and by consequent escape of blood, which displaced the connective tissue, pierced the rete mucosum, and accumulated under the horny layer of the epidermis. That this injury to the blood-vessels is independent of the glandular elements is shown by the implication of blood-vessels not in immediate proximity with these structures.

Duckworth made a microscopic investigation of an iodic pustule, and found that the superficial layer of the cutis vera was principally implicated. The papillary layer at the affected parts was flattened out, stretched, and even excavated, and contained a large number of small cells and a quantity of newly formed fibrous tissue. The blood-vessels were numerous and enveloped in sheaths of exudative corpuscles; no evidence of the rupture of any blood-vessel was to be obtained. The sweat glands seemed entirely unaffected, even in close proximity to the pustules. There was no implication of the hair follicles. He infers from this that the lesions are not of the nature of acne, but are due to a superficial localised dermatitis resulting in cicatricial tissue.

Farquharson attributes a marked influence in the production of iodic eruption to defective elimination of the drug, thus allowing it to remain longer in contact with the tissues of the body. This view gains support from the fact that the severer forms of the eruptions have sometimes been found associated with grave cardiac and renal disorder and the presence of albumin in the urine. The irritative effects of the iodide of potassium on the skin are, it is alleged, often corrected by the simple expedient of giving larger doses, which stimulate the kidneys, causing enuresis and a more rapid elimination of the drug from the system. Whether the potassium combined with the iodide contributes to promote the functional activity of the kidneys has not been definitely determined. Incidentally, it may be stated that patients treated at the Hot Springs of Arkansas often take large doses of iodide of potassium, as much as one ounce per diem, without liability to incidental bad effects. The copious use of the waters, both internally and in the form of baths, no doubt produces a hyperactivity of the sudoriparous glands, as well as the kidneys, and the consequent rapid elimination of the drug.

It is worthy of note, however, that the retarded elimination of the drug does not explain the occasional occurrence of eruptive accidents within a few hours (four or five) after the ingestion of a single insignificant dose. This fact also contravenes the fanciful theory that iodic eruptions are in

all cases the outward expression of evidence of a saturation of the system with iodide of potassium—an opinion formerly held by a majority of authors.

*Diagnosis.*—Certain forms of the iodic eruption may be confounded with variola and syphilis. The shot-like papules which precede the development of bullæ were said by Hutchinson to resemble those of the early stage of variola, but as they run their course rapidly the diagnosis is soon easily made. The occasional appearance of umbilication, caused by the vesicles spreading at its margin and sinking in the centre, is an element of confusion. The exudation is sometimes so free that crusts form not unlike those of syphilitic rupia. Other forms have been mistaken for syphilis, and iodide of potassium may be continued, possibly in increasing doses, for the very condition which it has caused. Fox says, "I have often been consulted for supposed syphilis, when the disease has been simply an iodide rash."[1]

### *Tests for Iodine and Iodides.*

When the quantity in the urine is small, and other tests produce doubtful results, it is necessary to eliminate organic matter by the method detailed under bromine, in which the disulphide of carbon will acquire a fine violet colour if iodine was present.

If notable quantities of iodine are contained in the urine, it is often possible to detect it by one of the following methods:

1. To detect iodine in the urine, the compound is first to be decomposed by fuming nitric acid and dilute sulphuric acid, then a little starch paste, and a few drops of the sulphide of carbon are to be added, whereupon a beautiful blue colour appears. On shaking it, a small portion of the iodine is dissolved by the bisulphide of carbon, and a dark-blue

[1] A case in point is the very severe tuberose eruption figured by Hutchinson in the 'Archives of Surgery,' July 1889. Pye-Smith observed in a patient suffering from an ordinary pustular syphilide that some of the lesions on the face and back of the hand became hypertrophic and warty under the influence of iodide of potassium.—T. C. F.

ring of iodide of starch is formed on the layer of bisulphide of carbon.

2. A less reliable method is as follows :—After starch paste and dilute nitric acid have been added to the urine, a few drops of fuming nitric acid are added, when a blue colour appears, which on heating disappears, and returns again on cooling.

3. After sulphuric acid and fuming nitric acid are added, the fluid is shaken with chloroform. Then occurs, through solution of iodine in the chloroform, a violet colour.

4. Sometimes the iodine is in such combination that the above agents do not free it, and it may be necessary to add chlorine water for this purpose, or the urine may have to be incinerated and then tested.

*Treatment.*—The treatment consists in the suspension of the drug until the eruptive accidents have disappeared. Various expedients have been suggested with a view of preventing the occurrence of the untoward effects of the drug while continuing its use. Arsenic in the form of Fowler's solution, two to ten minims with each dose of the iodide, has been recommended, and tried in some cases with good results. Paget recommends aromatic spirits of ammonia. Aubert has recently recommended belladonna as a means of preventing the disagreeable effects of iodide of potassium. Fournier recommends that the iodide be administered with claret. According to Keyes, tolerance of the drug may often be secured by giving it in a glass of milk or large quantities of Vichy. As mentioned above, intolerance of the drug may sometimes be overcome by simply increasing the dose. It will be found that a single dose of two or three scruples in a cup of tea at bedtime is less liable to produce irritative effects upon the skin than a less quantity taken in a little water in divided doses. If evidences of the so-called "supersaturation" appear, the drug should not be again administered for four days, as that period is required for its complete elimination. Besnier claims that the drug introduced hypodermically does not give rise to the same accidents as when introduced by the stomach. A more extended clinical experience on the part of others has not verified this claim. Free use of acetate of potash and

remedies of this class is to be recommended with the view of charging the system with an abundance of alkali, which may combine with any free iodine that may be present.

Ehrlich has extolled the value of sulphaniline as a prophylactic, as well as a corrective measure after symptoms of iodism have been developed. As soon as the iodism appears a dose of four to six grains of sulphaniline is given, followed by smaller doses, often repeated if necessary. The success in many of these cases, he claims, is remarkable, well-marked, and even exaggerated symptoms, being removed in some cases by a single dose, and after-tolerance being established. In other cases the results were not so decided. No bad results were observed from this treatment.

### IODOFORM.

The cutaneous irritation which sometimes follows the external application of iodoform is doubtless due to the contained iodine. It may result from dressings of iodoform gauze, or the use of the drug in powder, in ointment, or in solutions of ether, or from its absorption from the mucous surfaces of the vagina and rectum when used in the form of suppositories or injections. The eruption is usually of an erythematous character, but the inflammation may proceed to the development of vesicles and bullæ. In an examination of the literature of iodoform poisoning Cutler found numerous references to eruptive accidents developed in connection with other toxic symptoms. They consisted ordinarily of simple erythemata or papular eruptions sometimes covering the whole body. The eruption usually disappeared rapidly upon leaving off the iodoform.[1]

[1] R. W. Taylor, in 1887, reported on twenty-five cases of iodoform eruption, nine of them personal. He found that toxic effects were most frequently manifested by systemic troubles without cutaneous changes. In sixteen cases of eruption constitutional symptoms were present; in nine a rash occurred without systemic symptoms. In order of frequency the eruption was *erythematous* (simple, papular, vesicular, bullous) or *eczematous*, or rarely *purpuric*. So strong may be the idiosyncrasy that an eruption may follow the simple smelling of the drug. The eruptions are characterised by prompt invasion and rapid extension, either commencing at the point of application or at various centres. These general manifestations

Zeissl records two cases of iodoform rash. In one case, in which an iodoform dressing was used, there appeared over the skin of the body, flexor surfaces of the arms, and the inner surface of the thighs an erythematous eruption of a diffuse bright-red colour, disappearing under pressure. In the second case the eruption was consecutive to the introduction of iodoform pencils into a sinus every second day. On the tenth day there was itching of the extremities, followed by the appearance upon the skin of the body and extremities of an eruption of urticaria nodules of a reddish colour, from the size of a lentil to that of a three-cent piece.

Hoepfl reports a case in which an exanthem of small red spots covering the entire body was caused by an iodoform dressing to an amputated breast.

Neisser records eight cases of iodoform rash, characterised by the formation of small vesicles, and closely resembling acute eczema. In a few hours after the application a deep redness of the surface comes on, accompanied by violent burning and itching; then vesicles filled with clear fluid appear, and soon form crusts. In some cases the wounds dressed with iodoform took on an apparent erysipelatous action. In two of Neisser's patients a tormenting eczema of the anus and perinæum was caused by the use of iodoform suppositories. In two cases of females similar eruptions broke out over the inner surface of the thighs whenever iodoform had been applied to the vaginal orifice.[1]

Fabret observed an eczematous eruption in a syphilitic subject provoked by the application of an iodoform ointment.

Taylor holds, in agreement with Neisser and at variance with J. C. White, are not to be confounded with the local dermatitis due to the direct local contact of iodoform (especially the crystalline drug) as frequently seen on the face and hands of dressers, &c. The problem is often somewhat complicated in the case of iodoform by the diffusibility of the powdered drug and its possible transmission by scratching, &c. This complication has, however, been most carefully eliminated in many cases.—T. C. F.

[1] It is to be noted that although a remarkable idiosyncrasy existed with respect to iodoform, no accidents followed its internal administration. As far as I am aware, there is not any case on record of an eruption due to the ingestion or hypodermic injection of iodoform. Bolowski observed the occurrence of intoxication and an eruption after the introduction of a uterine suppository containing 1½ grains of the drug.—T. C. F.

Treves reports a case of iodoform exanthem which was somewhat peculiar in its mode of development. After iodoform had been used for three weeks to a wound of the forearm the entire member became red, swollen, and œdematous. On the following day a crop of vesicles, about thirty in number, appeared upon the forearm. The iodoform was discontinued, and the vesicles suppurated and healed up. Three days later a remarkable exanthem appeared, covering the arm and shoulder and greater part of the face, the sides of the neck, and frontal aspect of the chest. The eruption consisted of patches of closely packed minute papules seated upon an erythematous base. The patches varied in size from a sixpenny to that of half-a-crown piece. They were irregularly circular, with a clearly defined margin, and ran the one into the other. The eruption disappeared in two days.[1]

The production of the iodoform rash would seem to depend upon a peculiar susceptibility of the skin to irritant influences, as in many cases the slightest trace of iodoform in any application will cause the eruption to appear.

Köster-Syke reports his personal idiosyncrasy against iodoform, so marked that within a few hours after dressing a wound with an iodoform bandage he experienced a most intense itching over the entire body, attended with a slight elevation of temperature. The following night his face, hands, and arms to the elbow were enormously swollen, and the seat of a vesicular and pemphigoid eruption. On another occasion he used a little iodoform powder, this time taking the precaution to protect his hands with kid gloves. In ten minutes he experienced an itching sensation in the hands and face, and in a few hours the dorsal surfaces of the hands to the tips of the fingers, the face below the eyes, and the integument behind the ears were covered with itchy red points. A pronounced idiosyncrasy was also manifested in his case against carbolic acid.[2]

[1] This case demonstrated a fact, illustrated by others, that iodoform may be applied to a wound for some time without producing ill effects, but that directly the surface becomes favourable to absorption an eruption and often a systemic intoxication may occur.—T. C. F.

[2] Taylor applied iodoform to two small chancroids on the inner layer of the prepuce, and within three hours the whole penis and scrotum were red,

### *Tests for Iodoform.*

To separate iodoform from the urine it is best to subject the latter to brisk distillation, taking care to use a cold condenser. The distillate is tested in the same manner as directed for chloroform (see chloral) by applying the isonitril reaction. In addition, it is necessary to recognise the iodine

swollen, and the seat of intense pruritus and burning. The symptoms recurred on touching the sores, after an interval, with ethereal solution of iodoform. There was no systemic reaction. Campbell Pope dressed an inflamed bursa of the arm on three separate occasions, at intervals, with (1) iodoform gauze, (2) again with iodoform gauze, (3) with iodoform ointment. After each dressing an eczema-like dermatitis attacked the whole limb, Taylor dusted a bubo cavity with iodoform and stuffed it with plain gauze, retained by a spica bandage. On the following day an erythematous rash had spread nearly to the umbilicus and half way down the thigh. There was no systemic reaction. Marcus Beck dressed with iodoform a wound made by the removal of an atrophic scirrhus of the breast. Forthwith, an eczematous dermatitis spread continuously over the whole side of the thorax. Taylor dusted iodoform freely on some rupial ulcers on the left leg of a man in wretched health and bandaged the limb. Local irritation arose at once, and next day a deep red erythematous eruption had spread from the leg to the thigh, coincident with systemic poisoning. A scarlatiniform erythema appeared about the neck and shoulders, increased rapidly, merged with the invading erythema of the thigh, and in forty-eight hours covered the whole body. Wallich dressed a finger with iodoform for a month. Dermatitis then set in locally, subsequently attacked the other hand, and a rubeolar rash appeared on the forearm, arm, thorax, and abdomen. Janovsky dressed an ulcerated gumma of the left calf with iodoform, and in three days there was ephemeral febrile disturbance and dermatitis of the left thoracic region, the back and the left shoulder blade. The same observer dusted some iodoform over soft chancres. Febrile reaction occurred in two days, and an erythema appeared on the thighs, the right hypogastrium and lumbar region, extended to the left side, and then invaded the forearms. This experience was repeated. Gerlach dressed an ulcer of the leg with iodoform ointment (℥j to ℥j) spread on lint and bandaged. A few hours later the whole leg was swollen and the seat of bullous dermatitis. In twenty-four hours there was enormous swelling of the face, temples, and ears. In forty-eight hours there was swelling and papular eczema on the forearms, arms, neck, and upper third of the chest, and back.

*The Petechial Form.*—Janovsky applied iodoform to a scraped lupus patch of the right thigh of a girl. Three days later purpuric spots appeared over the surrounding skin, and continued to develop as high up as the breasts. Fourteen days later the drug was reapplied with a similar result —T. C. F.

forming one of its constituents. This may be done by adding to the liquid a little nitrous acid (prepared by acting upon starch with nitric acid and heat, and diluting with about an equal volume of water). On subsequently adding some gelatinised starch a tint varying from faintest purplish to blue will be obtained.[1]

### IPECACUANHA.

The prolonged application of ipecacuanha to the skin causes irritation characterised by redness, and the formation of papules, vesicles, and pustules, which, on healing, are not followed by pitting or scarring.

According to Baudot, the papules are large, few in number, red from base to summit, without circumferential areola. The lesions have no tendency to run together. They are intensely itchy, and from the scratching which they provoke, they frequently become covered with blood-crusts analogous to those of prurigo. They disappear slowly. According to Delioux, the pustules may be umbilicated like those produced by antimony. A diagnostic feature is that the former do not ulcerate and leave scars. The internal use of ipecacuanha may also occasion eruptive disturbances. Turner describes a case in which there was burning heat diffused over the whole surface of the body, together with a kind of erysipelatous eruption covering every portion, similar to what is seen after exposing the naked skin to a burning sun. Circular patches, with elevated, thick, and rounded edges, and of a fiery colour, characterised the eruption.

### NUX VOMICA. STRYCHNIA.

Dierbach, quoted by Piffard, says that strychnia internally administered will produce formication and pruritus, and a sensation as if the skin were pricked with needles, or there may be diaphoresis and a miliary eruption.

[1] Burlureaux confirms the tests of iodoform toxæmia given by Poncet that (1) a piece of silver placed in the mouth gives rise to a taste of garlic, (2) that when a pinch of calomel is mixed with the saliva a canary-yellow tint is produced due to the formation of iodide of mercury.—T. C. F.

Skinner reports a case in which one twenty-fourth grain of strychnia produced a scarlatinoid exanthem.

### OLEUM CADINI.

The oil of cade frequently excites inflammatory action when applied to the skin. The most common form is an erythematous and papular eruption, which may extend beyond the original point of application and involve a large extent of surface. This dermatitis may take on an erysipelatous form, through the implication of the lymphatic vessels in the inflammatory process.

A papular eruption presenting many features in common with tar acne is one of the forms of cade irritation. Baudot describes it as follows: the papulo-pustules are disseminated or united in groups, slightly confluent, but distinct from each other, implanted in the skin upon a large papular base terminating in an acuminate summit, and each perforated by a hair. The papulo-pustules are hard, solid, red, and surrounded by an areola of the same colour. The suppuration is localised at the summits. Since this eruption is most abundant and characteristally developed on the hairy parts, Bazin has designated it as *sycosis cadique*.

Kleinhaus says that the hair-follicles are projected above the skin in the form of nodules of the size of a hemp-seed. The susceptibility to the irritant action of the oil of cade varies in different individuals. Women are specially liable. Quite recently a woman, aged forty, came under my observation with an eczema affecting the forearms, wrists, backs of the hands, and interdigital surfaces. A single application of the oil of cade (one to seven of vaseline) produced an intense burning, itching, and swelling of the fingers and backs of the hands extending to the wrists. Two days later a number of large blebs were observed over the dorsal surface and sides of the middle and index fingers. The backs of the hands were enormously swollen, and the skin studded with a large number of pin-head sized vesicles. A week later the hand was still œdematous, and the epidermis had peeled off from the middle and index fingers.

with a yellowish crust. The crusts usually fall off within a week or ten days, leaving a coppery pigmentation. When the inflammation involves the true skin they may be followed by permanent cicatrices.

The volatile portion of the oil may occasion a dermatitis of neighbouring parts, or secondary vesicular eruptions may appear, particularly upon the face and genitals, from accidental transference of the oil by the fingers or otherwise. In some cases it would seem that secondary eruptions are consecutive to absorption. Trousseau observed an eruption upon the scrotum when distant parts of the body were rubbed with croton oil.

### OPIUM; MORPHIA.

The irritant effect of opium upon the skin has been recognised from the time of its introduction into the materia medica. While the older observers speak of an intense burning and itching as a frequent accompaniment of the use of this drug, it does not appear that they were familiar with its property of producing changes in the skin of an eruptive character. Dioscorides and Paulus Ægineta describe the *pruritus opii* as a tormenting and unbearable affection. Tralles, quoted by Lewin, published in 1774 the first observations relating to the eruptions produced by opium, which he regarded as due to increased sweating. Incidentally it may be said that Trousseau connects the opium exanthem with a modification in the sudoral secretion occasion by the drug, which alteration of secretion, he says, determines an irritable condition of the skin, resulting in erythematous redness and pseudo-measly patches, sometimes in vesicular eruptions, and even in veritable papules when the action of the medicament has been prolonged. The production of the eruption, however, bears no relation to the stimulation of the sweat-glands, as it may occur without any increase in this secretion.[1]

The most common manifestation of the irritant effect of

[1] Ringer also points out the powerful sudorific action of opium, and states that "the cutaneous emunctory is especially charged with its elimination." To meet the argument that the eruption may occur without any increase in the sweat secretion, Trousseau supposed that the eruption was due to a peculiar quality imparted to the sweat.—T. C. F.

opium upon the skin is an erythematous eruption which may occur as diffuse uniform redness simulating scarlatina, or it may be macular like that of measles, consisting of small isolated spots of a bright or dusky red. They first appear upon the face and neck and flexor surfaces of the body, and are preceded by a hot itchy sensation in the skin. Usually the eruption disappears promptly after discontinuing the medicine, and is followed by a slight desquamation.

Behrend reports a case of opium eruption which appeared after taking a few powders containing one quarter grain. It was a pale scarlatinoid eruption, which on near inspection was found to consist of minute papules closely studded, distributed over the chest from clavicle to end of sternum, upon the inner side of the arms, flexor surfaces of forearms and wrist-joints, spreading down the thighs and inside of knees, and terminating at the ankle in a stripe of livid colour. The pruritus was of so violent a character as to prevent sleep. The eruption subsided on suspension of the opium, but was promptly redeveloped on resuming its use. Desquamation of a branny character, foliaceous over hands and feet, occurred several days later.

Morod ordered pills of opium to a lady patient who declined to take them, declaring that every time she took opium it made her as red as a lobster. He prescribed instead *syrup diacode*. The next morning the patient was indeed red as a lobster, the eruption being accompanied with intense itching.

An exanthem resembling scarlatina has been observed on the face, neck, hands, arms, and legs of a lady patient after she had taken a single drop of laudanum. It has been observed that women are much more subject than men to the accidental irritating effects of opium.[1]

[illegible] also a case in which a single enema of laudanum was followed by a severe attack of urticaria.

[illegible] records a case of a man in whom an erythematous rash of a whole [illegible] subsiding of the part with an opiated ammoniacal liniment. The man had previously suffered from generalised erythematous rashes [illegible] use of opium and after hydrochlorate of morphia.

[illegible] feature of opium and morphia eruptions that where they [illegible] remarkable susceptibility to the drug in whatever way it is

## MORPHIA.

Intense pruritus, with or without eruptive disturbance, ay follow indifferently the ingestion or the hypodermatic troduction of this salt into the system. An exudative, ythematous eruption is the most frequent form of morphia uption.

Apolant reports a case of a man who, after taking twelve fifteen drops of a weak solution of morphia, equivalent about four drops of Magendie's solution, had an eruption red wheal-like prominences on the hands and other por- ons of the body. The eyelids were swollen and the whole ce œdematous. It was accompanied with intense burning d itching. Desquamation in large lamellæ occurred five ys later. The patient, who had been ignorant of the nd of medicine ordered, recognised it from having before d a similar experience.

Scheby-Buch reports a case in which the smallest doses morphine produced an urticarial eruption upon the face, est, and arms, and sometimes over the whole body.

Steinboemer records a vesicular eruption after one teenth grain of morphine. In the same patient one ghth grain of opium produced a similar eruption.

Comanos reports a case of eruption from the hypodermic jection of 0·02 morphia muriate. It consisted of an tense, uniformly diffused, scarlatinoid redness over the roat, breast, back, and left leg (the right was slightly ddened). Recovery took place in four days, with de- uamation of the epidermis.

The same quantity, given in pill form, produced a similar arlatiniform eruption over the entire body, accompanied th intense itching. Desquamation continued for several ys. Three weeks later, inunctions of morphia were used ree times daily for relief of sciatica. On the fifth day, ter thirteen inunctions, in which 0·05 morphia was used, e leg became reddened, and over places of inunction ere appeared small pustules and blisters. Then there peared three furuncles over the buttocks, the redness

d, and the eruptions will recur again and again under the influence of medicament.—T. C. F.

extended upwards on the back, and terminated in the formation of a large carbuncle, attended with high fever. Brivois observed, after the injection of 0·01 of hydrochlorate of morphia, a generalised eruption of discrete papules like those of prurigo, accompanied by intense itching. It was eight days before the papules disappeared. I myself have frequently observed an urticarial eruption after the hypodermic injection of morphia, which appeared indifferently after the use of small or large quantities.[1]

Surroville reports a case in which multiple ulcerations were caused by the ingestion of morphia. The use of the drug in increasing doses from five to twenty-five centigrammes caused dryness of the throat, loss of appetite, constipation, &c., soon followed by multiple ulcerations, both superficial and deep, with sharp-cut edges in the buccal cavity and pharynx. The ulcerations promptly healed after suppression of the drug. Again morphia was prescribed, and the ulcerations reappeared with more severity, accompanied by the same symptoms as before.

Hypodermic injections of morphia are frequently followed by inflammation and dermic abscesses, which may give rise to indolent ulcers persisting for a long time without showing any disposition to heal. Two such cases have recently come under my observation; in one, a chlorotic young woman, the ulcerations persisted for some months, and were finally healed up by strapping, with topical application of ung. iodoformi and internal use of potassio-tartrate of iron.

It has been observed that injections carried deep down into the subcutaneous tissues are not nearly so apt to be followed by phlegmonous abscesses as when the injection is discharged directly underneath the skin. It is also a matter of observation that hypodermic injections of morphia may be used for a long time without causing any local disturbance, when suddenly inflammatory reaction will

[1] Kirn ordered at midday a suppository containing ten centigrammes of the hydrochlorate, and next morning there was intense pruritus, with bullous erythema of the perinæum and scrotum and a general erythema. This patient had previously suffered from a generalised erythema, followed by desquamation after a hypodermic injection.

Mobius also observed a generalised erythema and urticaria following the use of a suppository.—T. C. F.

appear, not only in recent punctures, but in those which were made two or three weeks previous. Daniel reports an aggravated case of tubercular ulcerations from hypodermic injections of morphia frequently repeated during a long period. The arms were a mass of sores from the wrists to the shoulders; the legs in like condition from ankles to knees. The eruption was tubercular in form, many of the tubercles in a stage of ulceration, discharging a peculiar greyish matter, mixed more or less with blood and very offensive when allowed to remain for a time without cleansing the parts. The discharge was acrid in its properties, excoriating or scalding the surrounding parts painfully, leaving a wide-spread angry-looking surface which was especially marked on the patient's back and upper parts of the legs.

### *Tests for Opium and Morphine.*

If morphine alone is detected in the urine, or meconic acid and morphine, it may be concluded that the alkaloid has been administered in form of some salt (sulphate, meconate, &c., as the case may be). If meconin can be detected in addition, opium may be assumed to have been administered. It is best to first prepare an acid extract of the urine by evaporating it to one fourth, adding four times its volume of alcohol containing two per cent. sulphuric acid, filtering after twenty-four hours, and then evaporating off the alcohol. The residuary liquid is filtered when cold.

If this is shaken with two successive portions of benzin (about equal volumes), boiling at about 176° F., the benzin solution evaporated, and the residue treated with a few drops of colourless concentrated sulphuric acid, this will gradually assume a greenish tint, deepening to red in twenty-four hours, if meconin was present.

If meconin has been found, it is advisable to test at once for morphine. For this purpose the remaining acid liquid is rendered alkaline, and then shaken immediately with an equal volume of warm amylic alcohol, twice in succession. The alcoholic solution is evaporated, and the residue tested as follows:

A portion transferred to a watch-glass is treated with a few drops of diluted hydrochloric acid, evaporated to dryness below 120° F., the residue dissolved in a few drops of water, and then a drop of highly dilute solution of ferric chloride added (free from acid). There will be developed a fine blue colour. A drop of nitric acid upon another portion of the residue will produce an orange or red colour, destroyed by sulphide of ammonium.

A few drops of Froehde's reagent (concentrated sulphuric acid containing, in each cubic centimetre, 0·01 grm. of molybdate of sodium or ammonium) brought in contact with even traces of morphine assume at once a magnificent violet colour, which soon turns green, brownish green, and yellow, becoming bluish violet after twenty-four hours.

*Treatment.*—On account of the exceedingly evanescent character of the opium eruption, treatment is unnecessary. Bromide of potassium is said to prevent the irritant effects of this drug upon the skin.

### PHOSPHORUS—ACIDUM PHOSPHORICUM.

The stimulating effect of phosphorus upon the cutaneous circulation, producing flushings and other evidences of peripheric capillary expansion, is well known. More decided evidences of irritative action upon the skin occasionally follow its use. A bullous eruption has been sometimes observed.

According to Farquharson and Ringer, purpura sometimes occurs as a symptom of its toxic action, and is usually developed in connection with gastro-intestinal derangement,

### PHENACETIN.

The occurrence of an exanthem following the ingestion of this coal-tar derivative has been reported by Valentin. An anæmic woman, who had taken bromide and antipyrin for headache without much result, was given six decigrammes of phenacetin on two successive evenings. This caused great heat in the face. Eight days later a dose of one gramme was given at night, and two hours afterwards there was flushing of the face, an erythematous general exanthem, most marked on the arms and legs, and next morning a temperature of 38·6° C. The skin lesions were not larger than lentils, in part acuminate, and darker in the centre. There was no itching, and the rash disappeared on the following day.—T. C. F.

icterus, &c. This observation has been confirmed in my own experience with the drug.

Hasse reports a case of pemphigoid eruption which occurred in a young girl who had been taking phosphoric acid. It disappeared on cessation of the use of the medicine, and reappeared on its resumption.

### PIX BURGUNDICA.

The local effect of Burgundy pitch applied to the skin is that of a mild irritant.

It may cause, after prolonged use, an inflammation of the skin of a vesicular or pustular character, and which is apt to be persistent. Trousseau observed that a Burgundy pitch plaster, having caused the local development of a great number of vesicles, sometimes occasions a general eczema, at first acute, which may afterward become chronic.

Cazenave also alludes to its property of causing eczematous eruptions.[1]

### PIX LIQUIDA—TAR.

The external application of tar may cause an erythematous, papular, vesicular, or pustular eruption.

The tar acne, which so often develops in connection with the external use of tar, consists of small, hard, red nodules, which persist for a long time after the application of the irritating agent has ceased, usually requiring from three to four weeks for their complete involution. According to Hebra, the hair-follicles become inflamed and swollen so as to form papules of the size of hemp-seeds, or even as large as lentils. The eruption is readily distinguished from ordinary acne, in that a black tarry point always occupies the centre of each papule. Farquharson reports, as the

[1] Kuehn observed an erythema papulatum follow the application of a pitch plaster.—T. C. F.

### PIMPINELLA.

Kaufmann reports a case of urticaria resulting from twenty-drop doses of tincture of pimpinella. A repetition of the drug evoked the eruption a second time.—T. C. F.

result of an application of Ung. Picis Liquidæ to a patch of psoriasis, an intense inflammation of the sound skin over an area several inches in breadth. There was a greyish discoloration, indicating the formation of a slough, which accident was only averted by careful sedative treatment.[1]

The internal use of tar, says Anderson, occasionally produces a copious red rash upon the skin, accompanied by fever, nausea, and other evidences of digestive derangement. Waldeck reports a case of an erythematous eruption, rubeoloid and urticarial in character, which followed the use of this drug in the form of Guyot's tar capsules.

### PLUMBUM—PLUMBI ACETAS—PLUMBI CARBONAS.

The external application of the salts of lead in the form of solutions or ointments sometimes produces discolorations of the skin of a brownish or blackish character.

Foucaud de l'Espagne reports the case of a lady who was ordered the acetate of lead as an eye-wash; under the advice of another physician she was at the same time using sulphur baths for rheumatism. A black discoloration of the eyelids ensued, which spread over the surface of the cheek-bones, and was only removed after six days by washing the parts with infusions of herbs.

The internal administration of the salts of lead may cause an erythematous rash of the skin. Snow, quoted by Piffard, reports a case where the body became spotted with petechiæ from the internal use of the carbonate of lead.

[1] Crocker says, "In some people a very moderate external use will produce swelling, redness, heat, and pain, and sometimes itching; vesicles and bullæ may form. . . . . In a few cases papules of tar acne may break down and ulcerate.

"When absorption occurs from its vigorous inunction over a large surface, shivering, fever, nausea, vomiting, and diarrhœa may ensue, with olive-green urine, black vomit, and fæces."

Quite a considerable literature has arisen with regard to eruptions occasioned amongst workers in tar distilleries, and the various products separated as naphtha, creasote oil, naphthaline, carbolic acid, anthracene, pitch, &c.—T. C. F.

### PODOPHYLLUM PELTATUM.

Workmen employed in pulverising podophyllum find it extremely irritating to the mucous surfaces with which it comes in contact, as well as to the skin.

Winterburn states that workers in podophyllum peltatum suffer from a cutaneous irritation, affecting more particularly the scrotum and genital parts.

According to Bentley, the topical application of an alcoholic solution of podophyllum will produce rubefacient and vesicant effects.

### POTASSII BICHROMAS.

The extensive use of bichromate of potassium as a mordant in the manufacture of woollen goods is a prolific cause of dermatitis.

The irritant action of the bichromate is shown in the production of eruptions of a papular and pustular character upon the hands, forearms, and exposed parts of the body. Deep ulcers and sloughs not infrequently occur, with ulcerations of the mucous surfaces and perforations of the septum nasi, constituting the so-called "chromic disease" of the dyers.

Richardson reports five cases of eczematous eruptions in workmen who were employed in a manufacturing business where the bichromate was used in a watery solution of five or six per cent. The first symptoms of irritation are heat, itching, and tingling felt in the ends and middle joints of the fingers, which soon become covered with irregular red patches, upon which numerous minute elevations are seen clustered together. In the course of a day or two these enlarge into bead-sized vesicles. In a short time these clustered vesicles run together, forming large blisters, which rupture, causing the most acute pain and itching.

At this stage pustules begin to form over the body, mainly down the spine, neck, sides, arms, and ankles, accompanied with marked constitutional disturbance, as headache, fever, loss of appetite, &c. The eruption in some

cases presents, in addition to these cutaneous symptoms, the appearance of pityriasis rubra.

Harrington records a number of cases of bichromate of potash poisoning, resulting from the manufacture and wearing of caps, gloves, and other articles of clothing dyed with this substance.

One case was that of a strong healthy woman who worked in cloths used in making boys' caps. Her symptoms were intense itching of the hands, scalp, face, neck, and body. These were followed by ulcerations of the neck, breasts, hands, and thighs. The ears were much swollen, and became, as she expressed it, "running sores." The ulcerations about the nails resulted in the loss of three nails from one hand and two from the other.

Another case was that of a clergyman, sixty years of age, who wore a pair of brown woollen gloves. The dermatitis was limited to the parts covered by the gloves; it began with slight redness and irritation, "at first in the form of pimples, but afterwards many of them ran together forming blisters." These resulted in large and deep ulcers, many of them requiring over a month to heal. Symptoms of poisoning were also observed in two boys from wearing suits of brown woollen cloth. In all of these cases chromium was found to be abundantly present in the offending articles of clothing.

In large doses bichromate of potassium acts as an irritant poison, causing nausea, high temperature, sometimes suppression of urine and bloody stools. Few examples of cutaneous eruption are recorded from its internal use.

Quite recently, an eruption caused by wearing a greyish-brown flannel shirt dyed with bichromate of potassium came under my observation. The patient presented himself with an erythematous eruption surrounding the lower portion of the neck and covering the entire surface of the trunk and the arms, and extending over the buttocks and upper portion of the thighs.

About the neck and over the shoulders the eruption was fiery red, and upon the erythematous base were observed a large number of minute papules. The eruption, which had appeared two or three days previously, was intensely itchy

Its exact limitation to the portions of the body covered by the under shirt naturally suggested the nature of the irritating cause. Chemical examination revealed the presence of chromium in the colouring matter with which the shirt was dyed.

The eruption disappeared within a few days under the influence of a simple protective powder of oxide of zinc, bismuth, and starch.

According to Burness and Mavor, it may produce a papular eruption, which later assumes a pustular character.

Hughes states that the most characteristic effects of this poison upon the skin are seen in papules, pustules, and ulcers; the ulcers have hard bases and overhanging edges, are deep, and generally dry.[1]

Guntz, as is well known, claims the most remarkable beneficial results from the use of bichromate of potassium as a substitute for mercury in the treatment of syphilis.

### *Tests for Chrome Compounds.*

The only salt of chromium which has been administered internally is the bichromate of potassium. Yet chrome alum and other compounds are not infrequently used externally.

If chromium is to be looked for in the urine, the following method may be recommended for its detection.

Treat the urine with an excess of ammonia, heat it to boiling, replace the excess of ammonia if necessary; when cold, saturate the liquid with chloroform and set it aside for forty-eight hours. Pour off the liquid from any sediment; treat this with solution of soda, which will dissolve any chromic oxide present, and boil with an excess of brown peroxide of lead, whereby the chromic oxide is converted into chromic acid.

[1] Delpech and Hillairet established that the neutral chromate, and still more the bichromate, determines special lesions in workmen engaged in certain stages of the manufacture. Like arsenic, the powders produce rhinitis, peculiar and often severe ulcerations of the feet, hands, and scrotum, and papular and vesicular eruptions on other parts. Various animals exposed also suffer.

Besides those engaged in the manufacture of the chromates, and dyers, it may be noted that photographers, electricians, &c., are liable to be affected. —T. C. F.

Pour into a test-tube eight cubic centimetres of diluted and acidulated peroxide of hydrogen (commercial peroxide 5 volumes, water 24 volumes, hydrochloric acid 1 volume), pour upon it one half cubic centimetre of ether, and then add a few drops of the liquid, which should contain the chromic acid. If the latter was present, the upper portion of the aqueous peroxide layer will turn blue. On reversing the tube a few times without shaking, the ether will dissolve out the peroxide of hydrogen, and also assume a blue or bluish colour.

### POTASSII CHLORAS.

Although the internal use of the chlorate of potassium may cause irritant effects upon internal organs, especially the kidneys, it is not generally accredited with the property of producing cutaneous disturbances. The only references which I have found in medical literature relating to such incidental effects are the following.

Wegscheider reports, in connection with other toxic symptoms of the drug, the development of an eruption of red, non-elevated spots which became momentarily somewhat paler on pressure. They first appeared upon the arms and forehead, and spread, in the course of the following three days, over the entire body, becoming larger and of a copper-red colour.

In Stelwagon's case, the patient, a syphilitic, was ordered tablets, each containing five grains of potassium chlorate—several to be taken daily.

Four days later he returned with a "fiery erythematous and papular eruption over the neck and trunk, especially well marked over the upper part of the back." The tablets were not renewed, and the eruption, which was regarded as erythema multiforme, disappeared in two days.[1]

Six weeks later the patient was again ordered the tablets, and after using them for three days, an eruption, the same in

[1] Waldgemuth, after 150 grains had been administered over eight days, noted purpura on the legs and albuminuria.

Reynolds and Shote (quoted by Crocker) "noted bluish spots on the skin, sometimes a general cyanosis and sometimes an icteric tint, where poisonous doses of chlorate of potassium had been given."—T. C. F.

character as before, appeared; the trunk and neck were involved, and also several slightly raised erythematous spots were seen upon the legs. The eruption disappeared within forty-eight hours after discontinuing the use of the tablets.

Twice again, at the suggestion of S., who was desirous of testing the relation of the eruption to the drug, the patient took the tablets, and each time a similar eruption was developed.

### RHUS TOXICODENDRON—RHUS VENENATA—RHUS VERNIX.[1]

The irritating effect of rhus upon the skin depends largely upon individual susceptibility. While many persons are

#### RESIN.

Jacob attributed an urticarial eruption to this agency. A woman, aged 36, took about as much powdered resin as two walnuts for the relief of diarrhœa. Next day her face began to swell, and a papular eruption of urticarial nature appeared on the chest and arms.

#### RHUBARB.

Kuehn recorded a case of a generalised and desquamative recurrent scarlatiniform exanthem following the ingestion of rhubarb, ipecacuanha, &c., in the same individual. Goldenberg saw an instance in the case of a man aged 64. The eruption occupied the two cheeks, and was formed of reddish-brown pustules, of unequal dimensions, reposing on an infiltrated base, and forming in certain points, by their union, tumours, riddled with orifices and covered with thick crusts, and a similar eruption occupying the back of the two hands, reproducing itself on three different occasions after the administration of rhubarb. It was at first attributed to salicylate of soda, of which the patient made use, but its reappearance on several occasions after the employment of rhubarb did not permit any doubt of its real origin.

Litten, of Berlin, also recorded a case in a man of 45 some hours after taking rhubarb. There was rigor, fever, limb pain, and a visible papulo-pustular eruption generalised all over body and scalp and mucous membranes (mouth, pharynx, eyelids). After the development of the eruption all general symptoms went. The eruption was composed of hæmorrhagic taches of various forms, then pemphigoid pustules, confluent in certain places, and presenting then the aspect of foliaceous pemphigus. The lips were enormously swollen, were covered with pustules and bloody crusts.

The tongue was affected. Many recrudescences and profuse uretrorrhagia occurred. General state was nevertheless excellent. Twice before a similar eruption resulted after rhubarb. Litten, however, after cure, again gave infusion of rhubarb from another chemist, in case impurity was in the first. The same evening rigors were experienced, and a similar eruption occurred.—T. C. F.

[1] J. C. White gives the three species of plants growing abundantly in the

entirely insusceptible to its toxic action, others are so exquisitively sensitive that mere exposure to the volatile principle of the plant, without actual contact, is sufficient to cause the most violent cutaneous irritation. Curious examples of the remarkable potency of the poisonous emanations are vouched for on good authority, such as poisoning from walking through the damp grass in the vicinity of the plants, passing in the direct current of the wind blowing from them, sleeping in a chamber in which fresh ivy has been hung, exposure to the smoke of burning wood around which the ivy had clung, &c.

After exposure there is a period of incubation, varying from several hours to three or four days or longer, before the phenomena of cutaneous irritation begin to be manifest. The eruption is usually of an eczematous type. It is characterised by redness, sensations of burning and itching, and the appearance upon the erythematous surface of innumerable vesicles. The vesicles spread rapidly from the starting-point, if it be the fingers, along the dorsum of the hands, the wrists, and upwards along the arm. If the face be first affected, the inflammation rapidly involves the neck, and extends down the trunk towards the genitals.

The vesicles often run together, forming blebs of considerable size; these may be ruptured by scratching or otherwise, and expose large denuded surfaces, which soon become covered with thin crusts and scales. The contents of the vesicles are less limpid and transparent than in ordinary vesicles; sometimes, but rarely, they become purulent, absorption slowly taking place, leaving a slight pigmentation. The œdema and swelling of the integument assume an erysipelatous character, and occasion much disfigurement, especially when affecting the face. The rapid extension of the disease may be due to direct transfer of the irritating agent by the nails in scratching, or a systemic effect consecutive to absorption. The swelling of the glands which is so frequently observed in connection with rhus poisoning gives

United States as *R. toxicodendron*, or the poison ivy; *R. venenata* (*vernix* of Linnæus), or poison sumach; and *R. diversiloba*, or poison oak. A full account of rhus poisoning will be found in Prof. White's work, 'Dermatitis venenata.' Maisch isolated a volatile acid.—T. C. F.

colour to the probability of it being a phenomenon of absorption.

Lavini states that he applied two drops of the juice of rhus to the first phalanx of his index finger, leaving it on only two minutes, which produced, in about one hour, two black spots. Twenty-five days later he experienced a great burning in the mouth and throat, with rapid swelling of the left cheek, the upper lips, and eyelids. The night following the forearms swelled to twice their natural size, with a coriaceous skin, insupportable itching, &c.

Taylor brought before the New York Dermatological Society a patient who had had two attacks of an eruption presenting the characters of a dermatitis exfoliativa, from handling the twigs and leaves of the rhus venenata. The eruption commenced on his wrists and spread over the entire body; there was an abundant desquamation, and the lunulæ of the nails were affected, being wrinkled and thicker than natural. The second attack was experimentally produced six months later by rubbing the dried leaves over the left hand. Four days later he complained of itching and burning over the left deltoid muscle, the thighs, and genital organs. The conjunctivæ soon became reddened, and the entire skin was covered with large red blotches, which soon became diffuse, resembling a scarlatinal exanthem. The exfoliation was much slighter than in the first attack.

White observed in a pregnant female an eruption of papules and pustules upon the abdomen, arms, and dorsal surfaces of the hands from ivy poisoning. One of the pustules on the left arm attained the proportions of a well-developed boil. Confinement took place about the time the disease was disappearing. On the sixth or seventh day after birth there was observed on the child's belly an eruption identical with that from which the mother suffered. White regards this as an instance of the communication of a maternal affection to the child *in utero*.[1]

[1] Brown, of Pirbright, Surrey, called attention, in 1889, to the fact that the *R. toxicodendron* was becoming more widely distributed in English gardens. I have heard of several cases of rhus poisoning in the British Isles. Rhus poisoning is mentioned in several of the older books on botany and allied subjects. Prichard says there are eighty-five species of the genus *Rhus*, all more or less poisonous.—T. C. F.

Hubbard observed in a patient a vesicular eruption covering the whole body, attended with severe burning and itching, from eating a root of rhus which he had mistaken for sarsaparilla. The eruption differed from that produced by external contact only in the size of the vesicles, which were smaller.

The same character of cutaneous disturbance may follow the internal use of rhus in medicinal doses. Piffard reports a case of a female patient for whom he had ordered two-drop doses of the tincture of rhus to be taken morning and evening. On the third day he was called to treat the patient for erysipelas of the face, which presented all the characteristics of a rhus eruption.

Other observers speak of erysipelatous inflammations, pustules, boils, &c., resulting from the ingestion of rhus in small doses.

The rhus vernix, which grows in Japan, seems to be endowed with more marked irritating properties than either of the other varieties. A number of cases of erythematous and vesicular eruptions have been observed from the handling of Chinese lacquer-work, in the varnishing of which this variety of rhus is used.

In a personal communication from Dr. H. S. Allen, of Seoul, Korea, he states that natives as well as foreigners are often attacked with what is termed in that country "varnish poisoning." It comes on after contact with furniture or other articles recently varnished. Some persons cannot pass a furniture shop where articles are being varnished without being poisoned. His personal experience is thus related:—"My first eruption occurred in Nanking. The dermatitis first developed over my left eye, spreading to my forehead and nose; it itched and burned, causing great discomfort and inconvenience. Being ignorant of the effect of the Chinese varnish, I diagnosed the trouble as herpes zoster frontalis. The next attack was in Shanghai, after receiving a new chair from a Chinese cabinet-maker. The skin of the forehead became hot and itched intolerably, and was soon covered by an eruption of minute vesicles on a raised base. The swelling increased until the eyes were nearly closed. It

first diagnosed as a facial erysipelas, but consultation
g called, it was pronounced ' varnish poisoning.' "[1]
*reatment.*—The inflammatory changes in the skin met
in rhus poisoning are essentially the same as those
rmined by other irritating agencies, and the general
ciples of treatment indicated in rhus dermatitis will be
d applicable to other drug eruptions of an eczematous
. The various therapeutic measures which have been re-
mended may therefore be considered somewhat in detail.
s well to remember that in all these cases the inflamma-
is self-limited, with a tendency to spontaneous recovery ;
principles of rational treatment are to relieve the sub-
ive sensations of burning and itching, and to modify the
mmatory action.

With a view of circumscribing the spread of the eruption,
patient should be cautioned against bringing the hands
ontact with other parts of the body ; especially should
be enjoined against handling the genital parts, as the
gument of this region is peculiarly susceptible to the
ant action of the rhus. It is a matter of common
ervation that the genital parts of the male are much
e frequently the seat of the eruption than the corre-
nding region in the female, and the explanation is found
he direct transfer of the irritating agent by the fingers
handling the parts during the act of micturition, in
ssing, &c.

The treatment of the acute stage of the eruption should
essentially soothing and protective. For this purpose,
ting powders and sedative or mildly astringent lotions
uld be used.

The following lotion may be employed :—R Sodii Hypo-
phitis, ℥j ; Glycerinæ, ℥ss ; Aq., ad ℥viij. M. Apply
h compresses dipped in the solution and frequently
ewed. A strong solution of the sulphite of sodium may

[1] Junker says that almost all the workers in lacquer suffer repeatedly
a dermatitis. It may be accompanied by severe headache, dizziness,
r, coated tongue, sickness, irregular action of the bowels, congestion of
conjunctivæ and of the nasal mucous membrane. Those who sleep or
in a room in which freshly lacquered goods are drying may become
cted. The lacquer is made from the inspissated sap of the stem and
es of *R. vernicifera*.—T. C. F.

be used with benefit. In cases where the continuous application of a lotion is impracticable, freely dusting the surface with an absorbent powder is to be recommended. Pear's fuller's-earth, which is perfectly bland and unirritating, may be employed, or the following combination:— ℞ Pulv. Zinci Oxidi, ʒij; Pulv. Bismuthi Subnitratis, ʒj; Pulv. Amyli, ʒv. M.

It is important that the affected surface should be kept copiously covered with the powder; an occasional sprinkling does little good. If there is much burning heat present, a little powdered camphor (ʒss to the ℥j) may be added.

When the more acute eruptive features have begun to subside, a mild soothing ointment should be employed. For this purpose nothing is better or more universally applicable than the ordinary benzoated zinc ointment. Another very excellent dressing in this stage of the disease is the Lassar paste: ℞ Pulv. Zinci Ox., Pulv. Amyli, āā ʒij; Vaselini, ʒiv. M.

The good effects of the same treatment will be found to vary in different patients. There is a great difference in the susceptibility of different individuals to irritant action, and the difference in susceptibility is perhaps equally marked in relation to the influence of medication.

It is not possible to here enumerate the entire list of remedies which have been recommended in the treatment of rhus poisoning, for their name is legion. To give only a few which are claimed to possess a remarkable efficacy in subduing the symptoms: lime water, carron oil, alum curd, a saturated solution of bicarbonate of sodium, a strong solution of chlorate of potassium, a solution of sulphate of zinc (℥ss to the pint), a solution of carbolic acid (grs. ij—iv to the ℥j), a weak solution of sulphate of copper, dilute lead water, &c. Compresses to be wet with these lotions, and applied every hour or two through the day. Dr. White, of Boston, and others highly praise the efficacy of the ordinary black wash. Dr. Brown, U.S.N., claims that bromine (ten to twenty drops to the ounce of olive oil or cosmoline) is a specific.

To turn now to the vegetable materia medica: a decoction of white oak bark; a decoction of the bark or leaves

of the elder, an infusion of the sweet fern, the tincture or fluid extract of serpentaria, lobelia, sanguinaria, infusion of the bark of the red sassafras, with sassafras tea *ad libitum* internally, have all been highly spoken of. Probably the most efficient of the vegetable remedies is the grindelia robusta, which may be used in the form of the fluid extract, diluted in ten to thirty parts of water.

Dr. Hyde speaks enthusiastically of an ointment made by incorporating a decoction of the inner bark of the American spice bush (*Benzoin odoriferus*) with cold cream. Belladonna, the green vegetable bruised and mixed with cream, or in the form of the officinal ointment, has also been recommended. Dr. Edson highly extols the virtues of gelsemium in the treatment of rhus poisoning. His formula is—℞ Acidi Carbolici, ʒss; Fl. Ext. Gelsemii, ʒij; Glycerini, ℥ss; Aq. ad ℥iv. M. Cloths to be moistened with this lotion, and applied to the affected parts. This, he claims, with the internal administration of the fluid extract of gelsemium every three hours, effectually relieves the burning and itching, and the eruption speedily disappears.

Dr. White, of New York, recommends the following formula:—℞ Acidi Carbolici, ♏xx; glycerite of cocaine (4 per cent.), ʒij; vaseline, ℥j. M.; or ℞ Acidi Carbolici, ʒss; glycerite of cocaine (4 per cent.), ʒiv; Aq. Laurocerasi, ℥j; Aq. Rosæ, ℥ij. M. Either ointment or lotion to be applied several times daily. The plan of treatment found most serviceable in China for rhus dermatitis is, according to Dr. Allen, the constant bathing of the affected surfaces with an infusion made from freshly cut shavings of camphor wood. The officinal preparations of camphor were not found so serviceable.

### SANTONINUM—SODII SANTONAS.

Sieveking reports the occurrence of an eruption in a child after taking three grains of santonine. A wheal first appeared on the nose, and later there appeared an urticarial eruption over the entire surface of the body. A second dose of three grains promptly reproduced a general urticaria, attended with so much œdema as to render the child

unrecognisable. After a warm bath the eruption disappeared in the course of an hour or two.

Hubert observed in a number of patients who had been taking from ten to twenty centigrams of santonate of soda an eruption characterised by a large number of pin-head sized vesicles situated upon the trunk and limbs, but sparing the face. The vesicles never became confluent; they gradually shrivelled and disappeared, giving place to a slight epidermic exfoliation.

### SINAPIS.

The external application of mustard causes sensation of [illegible] and violent smarting, and, if the application be [illegible], vesication and even ulceration may result. According to Duchesne, pustules and violent [illegible] inflammation may follow. Rayer observed, during the course of the cholera epidemic in 1832, in a large number of patients, erythematous inflammations which lasted several weeks, produced by cataplasms of *farine de moutarde*.

### STRAMONIUM.

The demonstrated identity of daturia with atropia, the active principle of belladonna, would lead us to infer a similarity of action upon the skin. In the property of producing cutaneous disturbances, stramonium seems to occupy a position intermediate between belladonna and hyoscyamus, the two drugs with which it has such close botanical affinities.

The most common form of eruptive disturbance from the internal administration of stramonium is erythematous. The eruption is scarlatiniform in character, the redness bright and vivid, and attended with a sense of burning and itching.

Koch reports a case of stramonium poisoning in which the face and body were swollen, as if dropsical, and covered with a scarlatiniform rash.

Hegey records a case of generalised scarlatiniform eruption with pronounced angina, from the use of this drug.

Meigs observed from the use of stramonium hundreds of small brilliant petechiæ on the face, neck, and breast of a patient, many of which had a stellate form. An erysipelatoid inflammation has also been observed to follow the use of this drug.

### SULPHUR.

Sulphur exerts a stimulating influence on the skin. Strong applications cause irritation, characterised by redness, papules, confluent and painful vesicles. An artificial eczema is a common result of the application of strong sulphur ointment. The simple contact of the vapour in fumigations may produce a similar effect. Rayer says that he has often seen persons attacked with vesicular or papular eruptions after the employment of sulphur vapour baths.

According to Bazin, the sulphuret of potassium or sodium dissolved in water determines an intense irritation of the skin, which may be extreme if the strength of the sulphur be considerable, or the temperature of the bath elevated.

### SULPHONAL.

Engelmann reports the case of a woman, forty years old, a sufferer from metritis and dysmenorrhœa, who had been accustomed to taking, on account of insomnia, five tenths to one gramme (7½ to 15 grains) of chloral without evil effects. Sulphonal in two-gramme doses (30 grains) failed to produce sleep, but was followed by a diffuse scarlet eruption upon the outer side of both breasts. The eruption spread symmetrically and disappeared on the third day. It was attended by intense itching. The symmetrical arrangement suggested a central disturbance of the vaso-motor system.

Merkel observed a symmetrical eruption of small scarlet macules beginning in the axillary and inguinal folds, and spreading upon the outer surface of the shoulder and arm and on the thigh, the macules running together and forming large red patches. The eruption faded slowly, and ended by desquamation.

Schötten records a case characterised by nervine troubles and a morbilliform eruption following the employment of sulphonal in large doses.

Leloir mentions an eruption due to sulphonal constituted by a generalised macular erythema, localised chiefly on the thorax and flanks, and simulating a syphilitic roseola.

Lastly, Bresslauer observed in lunatics after prolonged sulphonal treatment great constipation, dark brown urine, slow, or in some cases rapid but feeble pulse, purpuric patches on the limbs, and great prostration.—T. C. F.

He observed as a result of four or five frictions over the lumbar region of four grammes of sulphuret of potassium to thirty grammes of water, a violent inflammation, characterised by pustules, dermic abscesses, and veritable phlegmons.

Baudot states that, under the influence of sulphur lotions and ointments, there results an irritation which is manifested by an active fluxion, quickly followed by a crop of very minute confluent vesicles, which are distended with a purulent or sero-purulent fluid, and surrounded by an inflammatory areola, two or three times the diameter of the vesicles; this eruption is quite painful.

According to Trousseau, the critical fluxion to the skin, known in technical language as *la poussée*, is a familiar phenomenon in patients who use thermal sulphur baths. It is manifested by small papules, and often a painful, confluent vesicular eruption.

The internal use of sulphur in medicinal doses often produces a dark coloration and much irritation of the skin, with eruptions of an eczematous character. Phillips has observed a red, papular eruption from the internal use of sulphur, and also, occasionally, boils and carbuncles. The waters of Harrogate, Barèges, Aix-la-Chapelle, &c., have been known to produce such effects.

De Schweinitz reports a case of scarlatinal rash which covered almost the entire surface of the body, especially well marked upon the face, chest, and neck, supposed to be due to the free use of flowers of sulphur in a gargle. It was observed that the exanthem grew worse after each employment of the gargle.

### TANACETUM—TANSY.

The only instance of eruptive disturbance from the internal use of tansy found on record is an observation of Porter. He observed a varioliform eruption in a young woman produced by the ingestion of one and a half ounces of oil of tansy, taken for the purpose of abortion.

### THAPSIA.

The application of this resin to the skin in the form of a plaster produces a rubefaction, accompanied by a very intense miliary eruption, analogous to that caused by croton oil.[1] Trousseau states that the eruption produced by thapsia differs from that produced by croton oil in the following points:—1, in its uniformity and regularity, all the pustules being alike; 2, in the large number of pustules; and 3, in the rapidity with which pus appears in the vesicles.

According to Tournadre, the redness and swelling produced by thapsia may be mistaken for erysipelas.[2]

I have seen a pustular eruption on the face from the application of a thapsia plaster on the chest for the relief of bronchial irritation.

### TURPENTINE—OL. TEREBINTHINÆ—TEREBENE.

The external application of turpentine causes irritation, manifested by sensations of burning and smarting, redness, vesicles, blisters, and other inflammatory changes. The vapours of turpentine may also produce a burning, itching, erythematous eruption. The dermatitis caused by oil of turpentine is often of an obstinate character, and may persist long after the cause which occasioned it has been withdrawn. It proves very intractable to treatment.[3]

The internal use of turpentine in medicinal doses may also cause eruptive disturbances of different degrees of

[1] The gatherers of this herb, and workmen employed in making the extract, are liable to dermatitis. J. C. White states that "if the action of the resin is prolonged the eruption becomes confluent, and leaves a suppurating ulcerating surface, with subsequent scars resembling those of smallpox."—T. C. F.

[2] The title of this thesis may be mentioned: "Des éruptions de la face consécutive à l'application des emplâtres de Thapsia sur le devant de la Poitrine."—T. C. F.

[3] Bürtzeff and Morel-Lavallée describe more or less generalised eruptions following local frictions with terebinthinate preparations.—T. C. F.

severity. The most common form is an intense erythema of vinous red hue, invading by preference the face and upper portion of the trunk. It may be accompanied by a profuse eruption of minute papules which often develop into vesicles, and then into pustules presenting a distinctly eczematous type. Brochin reports a number of cases in which an erythematous or urticarial eruption was observed after the ingestion of turpentine.

Berenguier reports a case in which large doses of the drug produced a scarlatina-like eruption, spreading over the face and upper part of the body in irregular patches; numerous minute acuminate papules covered the surfaces. The next day, the oil having been continued, the eruption spread to the lower limbs.[1]

As in the case of dermatitis from the external application of turpentine, the eruptions from its internal use manifest the character of persistency. Even after the eruption has disappeared, and desquamation has taken place, the subjective symptoms of itching and irritation may continue for an indefinite period.

Terebene, one of the derivatives of turpentine, likewise possesses the property of producing cutaneous irritation. Garland reports the case of a patient, aged sixty years, who took five-minim doses four times a day for chronic bronchitis. After taking six doses he had to desist on account of a profuse bright red papular rash, intensely itching, making its appearance first on the left hand, then on the ankles, extending up the legs to the knees. The patient had previously displayed an idiosyncrasy against turpentine. A turpentine liniment applied to a sprained wrist caused a

[1] Ernst Feibes observed a case in which, on the ninth day after the administration of 10·8 grammes of essence of turpentine in eight days for a gonorrhœa, there was intense pruritus and the evolution of acuminate, bright red papules over all the surface except the head and face, but mostly on the lower part of the trunk and legs. The rash disappeared three days after discontinuance of the remedy, but reappeared on the resumption of the drug in a more patchy œdematous form.

Gaucher records a case of generalised erythema with swelling of the face, extremities, and buccal mucous membrane. The rash appeared on the third day after taking ten to twelve capsules a day. Suffocative feelings were experienced. The erythema lasted four to five days.—T. C. F.

rash identical with that above described, and a swollen condition of the other arm.[1]

The presence of oil of turpentine, or of terpenes or camphenes in general, is chiefly recognised by the peculiar odour of the urine. It is often possible to distinguish the source in this manner.

### VERATRIA AND VERATRUM VIRIDE.

Although veratria is commercially derived from another source than veratrum viride, it will be convenient to consider together their irritant action upon the skin.

Veratria, which is rarely used internally, causes, when applied to the skin in the strength of the ordinary ointment, sensations of tingling, smarting, and increased heat, not only at the point of contact, but on remote parts of the body. When applied in a concentrated form it is highly irritant, producing erythema, and even pustular and petechial eruptions.

Veratrum viride is also irritant to the skin, its local application causing redness and burning.

The internal use of veratrum viride sometimes occasions an erythematous condition of the skin attended with sensations of pain. Forcke, quoted by Lewin, observed a pustular eruption on the face, most marked around the mouth.

The use of the drug hypodermatically is sometimes followed by painful swellings around the point of puncture, with extensive erythema. Eulenburg witnessed the formation of an abscess in one case.

[1] Lascelles Scott had a similar experience with terebene.—T. C. F.

### VALERIAN.

J. P. Frank describes the occurrence of an attack of urticaria invariably following the ingestion of eau de Seltz.—T. C. F.

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# CLINICAL AND ETIOLOGICAL RESEARCHES

IN

# PSORIASIS.

BY

LUDWIG NIELSEN,

SECUNDÄRARZT IN THE VESTRE HOSPITAL, COPENHAGEN.

TRANSLATED BY

FRANK H. BARENDT, M.D.Lond., F.R.C.S.Eng.

# CLINICAL AND ETIOLOGICAL RESEARCHES IN PSORIASIS.[1]

*The nature of the efflorescence.*—Hyperæmia is the first thing we notice clinically in the development of an efflorescence; the production of scales is a later feature. In addition to the frequent brown pigmentation seen especially after arsenic treatment,[2] *leucoderma* has sometimes appeared in the site of the efflorescence. This has also been observed after arsenic and large doses of iodide of potassium. The spots of leucoderma are usually quite small, but in some patients the patches are extensive, and have persisted unchanged for some months (at least six months).

*Localisation.*—The distribution of psoriasis in 862 cases was as follows:—On the trunk, extremities, and head, 489 times; on the trunk and extremities, 197 times; on the extremities only, 113 times; on the extremities and head, 53 times; on the head only, 5 times; on the trunk and head, 4 times; and on the trunk alone, only once.

Thus we see that limitation of the eruption to the *trunk* only is very rare indeed, and it is probable that this soli-

[1] The present paper is an abridged extract of a larger work ('Contribution to our Knowledge of Psoriasis,' Copenhagen, 1892, pp. 204, fifty-seven histories of cases, with index of literature), which I compiled during my three years' tenure of office as Secundärarzt at the General Hospital in the Department for Skin and Venereal Diseases (Prof. Haslund), from 927 cases of psoriasis (616 patients), extending over a period of twenty-five years, and from forty-three private patients in the practice of Prof. Bergh.

[2] In a case of Addison's disease dark brown pigmentation persisted after the spontaneous disappearance of the eruption.

tary case was one of eczema seborrhœicum. A few cases of psoriasis confined to the trunk are recorded by McCall Anderson. This circumstance is valuable in differential diagnosis, especially in the case of syphilis.

*Volæ* and (or) *plantæ* were attacked in 7 per cent. (65 times) of all cases (927), and in 8·9 per cent. (55 patients) of the 616 patients; but in 78 cases (66 patients) where we ourselves noted the smallest efflorescence this localisation was still more frequent, viz. 15 times (13 patients), or in 19·2 per cent. of cases and in 19·7 per cent. of patients. *This is much more often than is commonly stated;* of course syphilis was most carefully excluded. In one case only where the diagnosis of psoriasis seemed certain was the eruption confined to the palms and soles. On reference to the literature of psoriasis only two cases are recorded (Angel and Neumann) where the eruption was thus limited for some years, and afterwards appeared in the usual regions.

The volæ and plantæ were most frequently attacked where the eruption was very extensive or of the inveterate type. Sometimes, however, when it was slight or the first attack, these regions were involved. In two patients the palms and soles were attacked every time. The number of males predominated—54 males, 11 females,—possibly because of their greater exposure to mechanical irritation. Thus, in one patient who always carried his stick in the left hand, that palm was more affected than the right. The soles and palms were attacked 31 times simultaneously, the palms alone 24, the soles alone 10; both palms or both soles were most frequently affected. The diagnosis is not so difficult as is usually stated. It differs from syphilis especially in desquamation beginning in the centre of the efflorescence, the abundant formation of scales, and the very slight infiltration. Its course is similar to psoriasis in other regions.

*Psoriasis of the nails* occurred 8 times (7 patients) among 78 cases (66 patients), 10·2 per cent. of cases and 10·6 per cent. of patients. It was most frequently seen in extensive and old-standing (Ps. inveterata) psoriasis, and in the majority of cases the hands and and feet were implicated; the nail folds, palms, and soles likewise, but not invariably so. Males were most often attacked. There is nothing charac-

teristic in psoriasis of the nails, and there is no case on record where this was the sole localisation, and none is known where the eruption appeared afterwards in the usual regions (cf. psoriasis volæ et plantæ). The punctated condition of the nails is very frequent and characteristic (also seen in syphilis and eczema). It usually occurs in the finger-nails, and appears to be due to an affection of the matrix. Disease of the bed of the nail, with accumulation of scales under the nail extending from before backwards, is not uncommon, either alone or accompanied by the first-mentioned condition. The nails are also liable to other nutritive disturbances—atrophy, desquamation, and total detachment with subsequent regeneration. Psoriasis of the nails is amenable to treatment, and follows the course of psoriasis in other regions.

The glans penis and inner surface of the prepuce are not infrequently attacked (*balanoposthitis psoriatica*). The spots are sharply defined, red, glazed, and almost free from scales. Psoriasis started from the genitals in one case only. Of 270 cases of psoriasis of the head (and usually of other regions), face and scalp were attacked 127 times, scalp alone 104 times, face alone 39 times. That luxuriant growth of hair that has been noted sometimes was not observed. Psoriasis of *mucous membranes* was never seen.

*Causes of localisation.*—The general symmetrical distribution and the usual sites of the eruption support the view of external irritation symmetrically applied, *e. g.* pressure and friction of the clothing, irritation due to the occupation and habits of the patient, and the scratching from itching,[1]—com-

[1] The relationship has often enough been pointed out, as is seen in the sites of predilection (elbows, tubercle of tibiæ, shins, scalp, and sacral region). Several of our patients offered further examples of this connection. One suffering from kyphoscoliosis showed the eruption particularly well marked over the prominence of the spine. Another had psoriasis chiefly in the sacral region and over the prominences of the shoulder-blades; a third on his left knee, which he used most whilst working; a fourth over the left trochanteric region, on which side he always lay in bed; a fifth had the eruption more marked in the left palm than in the right, as he always carried his stick in the former; &c. In women the furrow caused by fastening the garments round the body is a favourite site. Scratch-marks are often attacked by psoriasis.

pare the causes of symmetry in scabies, in the dermatomycoses, &c. The assumption that the symmetry of psoriasis is the expression of some nerve-influence is no doubt purely theoretical.

*The beginning and development of psoriasis.*—The *initial localities* (in the first attack) are most often the extremities, viz. 130 times out of 182 cases. Of this number 130, the elbows, knees, and legs are especially stated to have been the seat 87 times, and then the scalp 18 times out of the 182 cases.

Although atypical in its *development*, various groups may be described, but with sundry connecting links. Out of 181 cases (first attack) the disease began 70 times (38·6 per cent.) as a *few scattered spots*, which remained practically unchanged for at least six months (often several years) without further extension. Eighteen of these patients never had an extension of the psoriasis, often of many years' standing, and it is perhaps not rare to find the disease limited to a small area. The localisation of these permanent patches was oftenest on the extremities, especially on the elbow and (or) knee 45 times, several times on one side of the trunk, 13 times on the scalp, and once only on the face. *Successive or quite acute outbreaks* occurred in 111 cases (61·3 per cent.). In 36 of these the eruption spread extensively in from five days to four weeks.

*The single exacerbation (or isolated outbreak) and the interrelationship of exacerbations (or separate outbreaks).*—Although an exacerbation of psoriasis follows no definite rule and then ceases, and although a remission may be very incomplete, or even partly coincide in point of time with a fresh attack, nevertheless fairly distinct exacerbations or isolated attacks may be recognised.

The *initial localisation* of later attacks appears on the whole to be the same as in the primary attack. In 65 cases where no efflorescence of former attacks remained, the extremities (elbow and knee specially noted 18 times) were first attacked 47 times, the scalp 5 times, the trunk 5 times, and various regions simultaneously 8 times. Owing to the influence of the predilection sites on localisation, the initial localisation and subsequent distribution of the eruption in

different outbreaks frequently recur in the same order in the same individual.

Further, the *method of progress of psoriasis* was generally the same as in the primary attack—in not a few cases it was acute: it followed no definite rule in the different outbreaks in the same patient.

*The localisation of the fully developed eruption* was frequently partially the same in the various exacerbations. Besides the predilection sites, the occupation and habits of the patient as well as the pigmentation after previous attacks may determine the site of new efflorescences. But apart from these factors, and without any other apparent cause, psoriasis often recurred in the same regions (sometimes in more unusual ones—face, genitals, palms) in the same individual without regard to severity of the eruption or the length of interval between it and previous ones. Conversely, in some individuals the more usual sites for psoriasis—scalp, back, and in two patients the elbows and knees—regularly escaped, though the outbreaks were frequent and severe.

The *distribution* of the eruption in the different attacks in the same individual appears to follow no regular course. Universal implication of the skin without any healthy areas intervening has only been seen in psoriatics suffering from *dermatitis exfoliativa, pityriasis rubra, herpétide exfoliative,*[1] &c. These differ clinically so much from psoriasis that they must be viewed as forms of dermatitis, often of varying pathogenesis, which complicate psoriasis, and into which psoriasis may pass. Such cases which may result from irritating treatment are also relatively frequent (comparing my own cases with the literature of the subject) in patients suffering from chronic alcoholism and chronic rheumatic joint affections. These diseases may be of importance in connection with dermatitis in psoriatics. It is, however, a somewhat rare affection, but liable to relapse.

A universal eruption (or almost so, with only a few healthy skin islets on the volæ, plantæ, and face), with the character of dermatitis exfoliativa, occurred once or oftener in 5

[1] *Psoriasis acuta vel ps. scarlatiniformis* cannot be sharply defined from *herpétide exfoliative* in psoriasis on account of the transition forms, as French writers, especially Brocq, state.

out of 520 psoriatics (779 cases). In 6 other cases the eruption was less extensive, but of the same character. Males were most frequently attacked by such a dermatitis; the 5 patients were all males (29—44 years of age, one 66 years old). Of the 6 that were less affected 2 were females (33 and 37 years of age). At least 4 out of the 11 patients were addicted to alcoholic excess, and got delirium tremens; one suffered from relapsing joint disease (chronic rheumatism) and heart disease (*v. infra*).

The dermatitis sometimes came on earlier, sometimes later in the course of the psoriasis, without apparent cause, and tolerably acute. The general condition was good, and no rise of temperature was observed. The eruption disappeared rather quickly (from twenty-four days to two months) on treatment, having previously existed at most three months in one patient. On some occasions, during the involution of this universal eruption, ordinary psoriasis guttata appeared. One patient appeared to have had two universal outbreaks before; another—an alcoholic with chronic rheumatism—had several serious attacks of psoriasis, having partly the character of dermatitis exfoliativa; and lastly, a heavy drinker had had seven such universal eruptions.

*The appearance and the special character of the exacerbation* are sometimes modified by the application of local irritants, *e. g.* irritant medicaments, or by the complication of other skin affections, or of general cachectic conditions (scurvy, syphilis, &c.). In some outbreaks infiltration, redness, and formation of scales were remarkably slight (*psoriasis pityriasiformis*) without apparent cause. *Psoriasis inveterata*, which presents quite opposite characteristics, appears rarely during the early stages of the disease, or as a first attack. It rarely occurred among our patients in a typical form, and was unaccompanied by any general disturbance. Sometimes psoriasis inveterata is met with in those suffering from chronic rheumatic arthritis (*v. infra*).

*Duration and course of the exacerbation.*—The average duration of treatment of outbreaks of psoriasis, cured with large doses of iodide of potassium up to 50 grms. daily (about 771½ grs.)[1] was in 27 adults 38·7 days; in 13 chil-

[1] The treatment of psoriasis with large doses of potassium iodide by

dren (under 15 years) 61·9 days; and with arsenic in conjunction with various external remedies (most frequently baths and tar preparations) was in 47 adults 52·3 days, in 9 children (under 15 years) 90 days. It is possible, had arsenic been pushed, that the cure would have been as quick as with potassium iodide.

From observation of our patients it may be stated *as a general rule, the average duration of treatment was much longer in the case of children than in that of adults.* This inference is not only obtained from the above figures, but also from the following statistics based on other methods of treatment (external remedies alone, and the internal administration of carbolic acid, &c.).[1] Thus the duration was in 107 adults 47·3 days; in 28 children (under 15 years), 74·7 days.

Further, out of 110 patients where treatment lasted at least three months and over, 21 were under ten years, 42 between ten and twenty years, and 47 above twenty years. On the other hand, of 55 patients where the eruption disappeared in the course of a month and under, there were only 2 under ten years, 8 between ten and twenty years, 45 above twenty years.

Psoriasis often disappeared remarkably quickly in *alcoholics,* probably because they were deprived of alcohol when in the hospital.

*The general condition* of the patient was as a rule undisturbed; in a few cases only subjective febrile symptoms were stated to have been present at the onset of the eruption. Elevation of temperature was, however, never observed.

No *disturbance of the bodily functions* occurred; *e. g.* the urine showed nothing abnormal, with the exception of a few cases where chronic nephritis was present, and once with diabetes mellitus.

In most cases the eruption was accompanied by *itching*—generally speaking very slight, occasionally severe. In universal outbreaks (dermatitis exfoliativa) constant chilliness without accompanying fever was sometimes observed.

Haslund ('Vierteljahressch. für Dermat. und Syphil.,' xiv, 1887, pages 708–9).

[1] Only cases have been used where no incidental complications required treatment.

Among our patients there was no affection present that could be regarded as a *true complication* of psoriasis. On the other hand, it was frequently met with in conjunction with other diseases (*v. infra*).

Herpes zoster, occasionally *arising during treatment* by arsenic,[1] must be mentioned, apparently caused by this drug, as well as a peculiar dryness and lustreless aspect of the skin of the palms (observed but once). During the treatment with potassium iodide, painful cutaneous and subcutaneous nodes, somewhat resembling erythema nodosum, but chiefly much larger (almost the size of an orange), developed in two patients—in one on two occasions he was thus treated. Besides these, several other more usual drug rashes were observed.

*The entire course of psoriasis* is quite *atypical*. In certain cases the disease lasts for years, sometimes for life, confined to the predilection sites. Exacerbations may cease at any period of its course, or even the psoriasis may disappear completely. We must, however, not ignore the possibility of a fresh outbreak. In some patients exacerbations occurred regularly once or twice a year for a series of years, frequently at definite periods. Sometimes long remissions or apparently complete intermissions[2] take place. The duration of the remissions varied: from one to five years, 49 times; from five to ten years, 10 times; and from ten to thirty-two years, 8 times.

Sufficient observations have not been made in order to determine how far remaining patches of psoriasis may influence a relapse. Lang's cases, treated with parasiticides till completely cured, favour the idea of such an influence; unfortunately their number is too small.

Forty-eight of our patients suffered from psoriasis with or without treatment from twenty or more up to fifty years. Only two of these, who had frequently been treated, suffered from psoriasis inveterata, and only a little over one third

[1] "The Appearance of Herpes Zoster during the Administration of Arsenic," by Ludwig Nielsen, 'Monatsh. f. prakt. Derm.,' xi, 1890, No. 7 (translated by the New Sydenham Society).

[2] On the parasitic theory of psoriasis we regard true intermissions in the light of complete recovery followed by re-infection.

had a very extensive eruption. Thus psoriasis, as a rule, shows no tendency to get materially worse even in untreated cases. On the other hand, in patients suffering from alcoholism and chronic rheumatism it is generally aggravated, and conversely intercurrent affections accompanied by profound disturbance of nutrition may be beneficial to, or even cure the disease (*v. infra*).

## II. Etiology of Psoriasis.

*Sex.*—Out of 520 patients suffering from psoriasis, 314 were males, 206 females—60·4 per cent. and 39·6 per cent. respectively. From a compilation of various statistics, out of a total of 2439 patients, 1482 were males and 957 females—60·8 per cent. of males and 39·2 per cent. of females, *a proportion* of 3 to 2.

*Age.*—Psoriasis is stated to have *begun* in 548 cases (325 males, 223 females)—

| | | | | | | |
|---|---|---|---|---|---|---|
| Before 15 years | . | . | . | 241 | times. |
| Between 15 and 20 years | . | . | 86 | „ |
| „ 20 „ 30 „ | . | . | 123 | „ |
| „ 30 „ 40 „ | . | . | 59 | „ |
| „ 40 „ 50 „ | . | . | 24 | „ |
| „ 50 „ 60 „ | . | . | 11 | „ |
| „ 60 „ 70 „ | . | . | 4 | „ |

Thus psoriasis began 241 times in childhood (under 15 years), *i. e.* 44 per cent., and only in 2·7 per cent. during the fiftieth year and upwards. Its appearance in the first five years of life was rare; one case only occurred in the second year: its frequency culminated between the fifth and fifteen year. It then diminished up to the twentieth year, and kept on decreasing materially during the succeeding decennia, exceeding the synchronous decrease in vital statistics.

The percentage was—

| | Males. | Females. |
|---|---|---|
| Under 15 years | 32·6 | 60·5 |
| Between 15 and 20 years | 14·8 | 17·0 |
| „ 20 „ 30 „ | 28·3 | 13·9 |
| „ 30 „ 40 „ | 15·1 | 4·5 |
| „ 40 „ 50 „ | 5·8 | 2·3 |
| „ 50 „ 60 „ | 2·8 | ·9 |
| „ 60 „ 70 „ | ·6 | ·9 |

The *percentage* of girls was almost double that of boys. From the twentieth year and upwards the excess of males was more than double that of females. Bearing in mind, however, that the proportion between men and women attacked by psoriasis is as three to two (*v. supra*), in order to state the relationship more exactly the percentage of males should be trebled, and that of women only doubled. This would considerably diminish or even abolish the difference in childhood between the two sexes if the element of uncertainty be taken into consideration. After the twentieth year, during the following decennia this difference becomes greater than the percentage calculation shows. *Among adults, therefore, the percentage of males attacked by psoriasis, as also the absolute number, are much greater than those of females.*

Neither *social status* nor any special *occupation* could be shown to have any influence over the manifestation of psoriasis.

As regards *heredity*, the result of our inquiries in 306 individuals showed that 218 times the patient was the only sufferer in the family, and that 88 times (28·8 per cent.) other members were also attacked. Out of the 306 individuals, the disease was directly hereditary 45 times (14·7 per cent.), indirectly only 7 times; 32 times, two or more brothers and sisters suffered; and lastly, in four cases details were not forthcoming. In 13 cases, besides psoriasis being directly hereditary, it was also present in several of the brothers and sisters of the patients.

It is very uncommon that all the children of one family should be attacked. Out of 320 children in 52 families (varying from 2 to 13 children in each family), where one or

more children had psoriasis, the disease affected 82. No rule of sequence for the evolution of outbreaks in point of time can be demonstrated among brothers and sisters, and they often get psoriasis at varying ages. The earlier manifestation or treatment of the disease, in contradistinction to syphilis, has no influence on its possible transmission to children.

Psoriasis appeared more frequently in childhood where there was direct heredity than where this was absent. Out of 43 patients whose parents or grandparents had had psoriasis, 24 were attacked before the fifteen year (55·8 per cent.) and 3 after the thirtieth year (6·9 per cent.). Out of 191 patients where the family history was free, 68 were affected before the fifteenth year (35·6 per cent.) and 40 after the thirtieth year (20·9 per cent.).

*At present there is no proof to show that the origin of psoriasis in several members of the same family should be explained by heredity; it may just as well at least be ascribed to contagiousness.*

*Relation of psoriasis to, and its complication with, other diseases.*—We have not been able to confirm the statement that psoriatics are endowed with particularly strong and healthy *constitutions* or an unusually fine skin. The statements of other writers to this effect are undoubtedly exaggerated.

If other diseases appear during psoriasis, they may either influence the skin disease or in turn be influenced by it.

*The relation of psoriasis to joint affections* has in recent years received considerable attention from French writers, although this had been pointed out previously. Space will allow us only to mention very briefly the cases of joint troubles that occurred among our patients.

Two individuals had gonorrhœal synovitis, and three acute rheumatism (one heart disease). None of these joint affections bore any relation to psoriasis. Five patients, of whom three were alcoholics, suffered from fugitive, afebrile—or almost so, highest temperature being 38° C. (100·4° F.)—rheumatic arthritis of one of the larger or smaller joints, without any relation to psoriasis, which showed nothing remarkable beyond simultaneity.

It has been especially stated that a certain relationship exists between psoriasis and *chronic joint disease.* One patient had chronic arthritis of the knee; and another (male, aged fifty-nine), with very slight psoriasis, suffered from arthritis deformans which began after the former. In neither case could any relationship be traced, and similarly in three other patients (all males, between fifty-three and sixty-five years of age) with chronic rheumatism or arthritis deformans, which had at least in two cases begun before psoriasis, in one as acute rheumatism. This patient had at the same time pyelo-nephritis, bronchitis, and emphysema. Psoriasis, which had lasted several years (seven to fourteen years) in the three patients, presented this relationship, inasmuch as it was of the *inveterate type,* and in two of them *very extensive.* Lastly, in three other patients *exacerbations of psoriasis* are said to have been *contemporary with joint troubles.* One of them (male, aged thirty-two) had chronic rheumatism which had begun twelve years before as acute rheumatism, and six years before psoriasis. The eruption was accompanied by loss of the finger-nails, and was very extensive. The second patient (male, aged fifty-five) had arthritis deformans which began two years after psoriasis of some nine years' standing. It was, especially at first, very extensive, and of the inveterate type; he also suffered from renal colic. Lastly, the third patient (male, aged forty-two), with psoriasis of nineteen years' standing (during the last ten years he had several exacerbations yearly, and was treated some twenty-six times in the hospital), had several serious outbreaks of psoriasis, partly of the character of dermatitis exfoliativa, once almost universal. He suffered from frequent relapses of chronic rheumatism of some ten years' duration. He had heart disease, and was a heavy drinker (delirium tremens).

In opposition to the view which French writers (Besnier, Brocq, &c.) hold concerning the relationship of psoriasis and joint affections, none of our patients furnished evidence of a neuropathic origin for the joint troubles, except in so far as arthritis deformans is generally regarded as neurotic.[1]

[1] Bourdillon, in a paper on 'Psoriasis and Arthropathy,' Paris, 1888, cites a fair number of cases of psoriasis (thirty-six) where joint and nerve

On the other hand, from a comparison of our cases of chronic joint trouble (chronic rheumatism and arthritis deformans) with those published by foreign, especially French writers, it appears that psoriasis *very frequently* but not invariably *develops severely, and often assumes the character of dermatitis exfoliativa or psoriasis inveterata.* Moreover the exacerbations of the skin and joint disease often, though not always, coincide, and both diseases may become aggravated in the same patient in the course of years. These points have also been insisted upon by French writers. But since both affections are liable to frequent exacerbations at definite periods of the year, no great stress should be laid upon their simultaneous occurrence. In most cases the joint affections began after psoriasis, corresponding to the different periods of life respectively in which they are generally met with.

From the number of cases where joint affections were present in the 616 individuals (927 observations), we are unable to conclude that arthropathies are frequently seen in psoriasis. The absence of figures showing the frequency of joint diseases in non-psoriatics, for the purposes of comparison, renders this point still more difficult of decision. We must further add that such patients are just those that more frequently come under observation, owing to the extensive character of the eruption. The approximate statement of Besnier and Doyon about the frequency of "arthropathic psoriasis,"[1] namely 5 per cent., not a little exceeds that derived from our patients.

affections besides some other complications were present. Without going into any details of the cases he tries to show that psoriasis and these diseases should be regarded as dependent upon the nervous system.

[1] 'Pathology and Treatment of Diseases of the Skin,' by M. Kaposi, 2nd edit., translated with additions by Besnier and Doyon, vol. i, p. 554. We are unable to accept this statement and its implied significance in the light of our own cases; a critical analysis of the literature of psoriasis renders its correctness, to say the least, very doubtful. According to our researches the relationship between psoriasis and arthropathy cannot be stated more precisely than the clinical connection mentioned in the text. Moreover a similar relationship is frequently found between other skin affections and joint troubles (eczema seborrhœicum, lichen ruber, primary dermatitis exfoliativa, &c.). Further, we consider Besnier's "psoriasis douloureux" (*v.* Bourdillon, loc. cit., p. 81) open to grave doubts. After

*Relation of psoriasis to acute diseases.*—Like many other skin diseases (lupus, scabies, favus, &c.), psoriasis may recede or even disappear during intercurrent febrile affections (*e. g.* once with pleurisy and twice with typhoid fever). In one patient psoriasis was of many years' standing, and very intractable to treatment. Such cases are scattered up and down in the literature of psoriasis. This coincidence is, however, by no means regular.

In a few cases psoriasis appeared for the first time immediately after an acute illness (scarlatina, measles, typhoid fever, erysipelas, and pleurisy). Cazenave has recorded a case where psoriasis attacked the recent pits after smallpox. Here, again, it was probably only an accidental coincidence.

*Relation of psoriasis to chronic diseases.*—Psoriasis may disappear in chronic *wasting diseases* (cancer, diabetes, &c.), and not recur (F. Hebra's case of recurrent hæmoptysis). Even this is not without exception, for psoriasis persisted in two of our patients who had incipient phthisis, and in another with cancer of the breast. On the other hand, we have never seen or read of psoriasis in advanced phthisical patients.

Chronic bronchitis, chronic nephritis, chronic gastro-enteric catarrh, chlorosis, and other chronic affections exerted no influence over psoriasis. Three of our patients had had ague. Poor's statement that malaria frequently occurs in psoriatics must depend upon the circumstance that his cases came from a malarious district (Hungary), and consequently were simply examples of coincidence.

Just as we were unable to find any ground for a neuropathic origin of joint troubles in psoriatics, so we are unable to confirm from our cases the statement made by some writers (especially Polotebnoff and Bourdillon) that the *nervous system* was so frequently implicated as to admit of

all it is not remarkable that patients submitted to frequent and daily baths (to which they are unaccustomed in the majority of cases) should at times complain of lumbago, stiff neck, and other indefinite rheumatic pains. The altered conditions of the skin would probably predispose to such affections. This has also been our experience with psoriatics, and it occurs in other diseases under similar treatment. In this connection acute sore throat appeared no less than thirty-three times. Twice only was true neuralgia noted.

a possible relationship between it and psoriasis. On the contrary (Prof. C. Lange and others), neuro-pathologists write that psoriasis seldom occurs in their practice. With the exception of a few cases of herpes zoster (during the administration of arsenic—*v. supra*), neuralgia is said to have occurred twice (ulnar and sciatic nerves). Affections of the cerebro-spinal system among the 616 psoriatics were as follows :—syphilidophobia with insanity occurred once, epilepsy four times, epileptiform attacks (due to alcohol), three times, hysteria once, disseminated cerebro-spinal sclerosis once, syphilis of the brain and spinal cord twice : and vertigo twice in one of the latter, doubtless due to arterial degeneration. These various diseases sometimes appeared before or after psoriasis without any apparent connection.

*Chronic alcoholism* undoubtedly aggravates long-standing psoriasis ; the most extensive and recurrent cases of psoriasis are most often met with in heavy drinkers, and alcoholism certainly favours the development of universal attacks (dermatitis exfoliativa, *v. supra*). In some alcoholics, however, psoriasis is but slight, and not specially liable to relapses, so that the rule is not without exception. As mentioned above, in some cases psoriasis disappeared rapidly when the alcohol was withdrawn.

*Relation of psoriasis to diseases with skin eruptions.*—Psoriatics do not appear to be less prone to other skin affections, and although this is questioned (F. Hebra and Neumann), it has been seen in individuals with *prurigo* (Neumann) and with *ichthyosis* (van Haren-Noman). Those cases are particularly interesting from a diagnostic, etiological, and prognostic point of view where a *local combination of psoriasis and other eruptions* exists (which is, however, not unusual in other skin affections). Psoriasis either attacks or starts from the site of a disappearing efflorescence of another skin disease, and *vice versâ* where the psoriasis efflorescence is the site or starting-point of the new skin disease.

Of the cases in which *psoriasis was secondary to another skin affection*, those are most interesting where *psoriasis appeared for the first time.* In two of our patients psoriasis

(first outbreak) is said to have attacked the site of *erysipelas*. In three cases recorded by Biart,[1] psoriasis (first outbreak, and no hereditary predisposition) began in the regions most attacked by *scarlatina*. Cazenave's case of psoriasis (first outbreak, no hereditary taint) after *smallpox*[2] has been already mentioned. Those cases are very remarkable where psoriasis appeared for the first time *after vaccination at the seat of inoculation*. Neither of Rohé's patients had had psoriasis; there was no hereditary predisposition, and animal lymph was used. In one of them the vaccination did not take; but from eight to nine days later a spot of psoriasis appeared in the site of inoculation, and a few days after numerous others elsewhere. In the other case it developed after the vaccine scab had fallen in the hyperæmic area, and shortly afterward the efflorescence generalised. Hyde is said to have seen a similar case.

Piffard gives a similar history of a case where psoriasis first appeared on the site of inoculation; the vaccination with animal lymph was also unsuccessful. Wood saw two sisters both vaccinated successfully with animal lymph, in whom psoriasis for the first time broke out after the pustules were healed: a brother had psoriasis.[3]

Chambard[4] records also a case of psoriasis (first outbreak) where it manifested itself after vaccination with animal lymph, in a child whose parents were quite healthy. Gaskoin[5] says he has seen six cases of vaccination where psoriasis began at the site of inoculation during the healing process; and Campbell[6] also mentions a case under similar circumstances.

In individuals who have *previously suffered from psoriasis* it is not uncommon to find it complicating other skin diseases, *e. g.* retrogressive eczema (Neumann, &c.) twice (among

[1] Mentioned in 'Annal. de Derm. et de Syph.,' 1883, p. 721.

[2] "Squamous Affections of the Skin; Psoriasis; Lepra vulgaris," 'Annal. des mal. de la Peau et de la Syph.,' vol. i, 1844, p. 99.

[3] Of several of these cases which were seen in North America (viz. Rohé's, Hyde's, Piffard's, Wood's) we have only been able to see the reference in 'Annal. de Dermat. et de Syph.,' 1883, p. 720.

[4] 'Annal. de Derm. et de Syph.,' 1885, p. 498.

[5] 'On Psoriasis or Lepra,' 1875, p. 49, and appendix.

[6] 'Archives of Dermatology,' July, 1877.

other patients), *seborrhœa congestiva faciei* once, *erythema nodosum* two cases (in one, perhaps, it was a first attack of psoriasis), *herpes zoster* once, and *urticaria* (Cazenave), &c.

In others the *psoriasis was primary, and the other skin diseases were secondary.* Such are those rare cases where an irritated psoriasis efflorescence has become the seat of *infective processes* (erysipelas, lymphangitis, and formation of multiple pustules in one of our cases). In other cases psoriasis has assumed an eczematous character as a result of irritation of the shins and other isolated regions (*psoriasis eczemateux* of Devergie, and *psoriasis arthritique* of Barin). Eczema seborrhœicum must be carefully differentiated in such cases. It is, perhaps, more correct to speak of an artificial *eczema* or *dermatitis* complicating psoriasis. The appearance of the former on the legs is also favoured by the greater chronicity of the psoriasis eruption, as well as by the itching due to the sluggish condition of the circulation (varix). Of course the inflammatory agents (probably micro-organisms) which we assume to be the cause of psoriasis may themselves be responsible for the increased irritation (Unna). On the other hand, we cannot assume, as Campbell does, that there is a close connection between psoriasis and eczema. *Dermatitis exfoliativa* occurring in the course of psoriasis may be regarded as more closely allied to eczema.

In several cases the skin, especially that of the scalp, forehead, face, at times chest and back, shows dirty yellow greasy scales, and in other places the typical efflorescence of psoriasis. These and similar characters not infrequently seen in syphilis should be rather viewed as a combination of psoriasis and *eczema seborrhœicum*, as Unna proposes.

The localisation of *papular syphilides* on psoriasis patches has been mentioned by Dornig and Neumann. In two of our patients *grouped ulcerative syphilides* appeared at the margin of extensive patches of psoriasis. The former disappeared on treatment with mercury ; the latter remained uninfluenced (as in Neumann's two cases). The exanthemata also show a predilection for psoriatic areæ (*variola*, Kaposi).

In one case *keloid* (Purdon) has been observed in patches

of psoriasis. Those rare cases where a psoriasis efflorescence has been the *starting-point of malignant neoplasms* are of importance from a prognostic point of view, *e. g. mycosis fungoides d'Alibert* (Pick and De Amicis) and epithelioma (one case Cartaz, two cases White, one case Hans von Hebra). In Hebra's and White's cases there were numerous firm *wart-like growths*, which developed in the patches of psoriasis on the extremities, and especially the hands. In fact, they formed the precursory stage, lasting some time before their malignant character set in. In all these cancer patients psoriasis had existed for many years, and none of them were particularly young, as often is the case with cancer developing from lupus (Ludwig Nielsen). Only in one of our cases was there cancer (of the breast) which apparently had no local relation to psoriasis. Cancer occurs so rarely in psoriatics that no "rapport de succession" can be traced between the two diseases.

*Relation of psoriasis to external irritation.*—Transient *mechanical irritation* may cause psoriasis as well as the persistent application of irritants. Köbner's case is well known with localisation of psoriasis in excoriations, the bite of a horse, and tattooing. Other cases are recorded where pin-scratches, the marks made by wet cupping, scraping with Volkmann's spoon, the pressure of a bandage, and even finger-nail scratches, have been followed by psoriasis.

In many cases efflorescences may be produced at will (*psoriasis factitia*) in a psoriatic by *scratching the upper layers of the epidermis* (Köbner's experiment). This was tried in forty-two of our cases; fifteen yielded a positive, twenty-seven a negative result. In almost all of them the psoriasis was still developing; the few times the scratch was made during subsidence of the eruption no result followed, and the same happened in those patients under treatment, although the experiment had succeeded before. In one case where the arm and chest were scratched, the former gave a positive, the latter a negative result. All the patients except two (both with a negative result after scratching) were treated with large doses of iodide of potassium. A positive result was first noticed *in some eight to ten days; slight punctiform efflorescences of psoriasis* appeared in the scratch-mark itself,

and later on they became confluent. The experiment apparently only succeeds, as Kaposi and Haslund observe, when the psoriasis is progressive, and in certain cases only. On the other hand, if the psoriasis is stationary or retrogressive it fails. Köbner has found this experiment useful in distinguishing psoriasis from squamous syphilides, as efflorescences never appear after scratching in syphilitic patients.

*In a few cases psoriasis began for the first time after and at the site of mechanical irritation*, in two cases after wet cupping (Veiel, Bazin), in one case under the pad of a truss (Kopp) with extension during the following weeks; in four of our patients after and at the site of injury. The data in this respect are somewhat defective.

*Chemical and thermal irritation* can also produce psoriasis efflorescences—blisters (one of our patients), sinapisms, cauterisation with caustic potash or argentic nitrate, burns (one of our patients), at times lotions, Turkish baths, &c. *On some occasions the primary attack of psoriasis has occurred after such irritation*—after the application of iodine to a contused knee with subsequent extension of the eruption (Wutzdorff), around a burn on the arm with subsequent extension, and in a recent scar from a burn on the forehead (Engelsted). In one of our patients (a healthy male about twenty, without any hereditary taint) the first outbreak occurred on the neck immediately after the application of hot fomentations for a sore throat. For eight days the psoriasis was confined to the face and neck, but after a warm bath numerous spots of psoriasis appeared all over the body in the course of a few days, though the patient was now well.

This relation of psoriasis to irritation, which is intimately connected with its appearance after the different exanthemata, is also observed in other skin diseases (urticaria, eczema, lichen ruber, lupus, dermatomycoses, &c.), if not quite in the same manner.

*Relation of psoriasis to physiological conditions.*—No close connection has been observed among our female patients between psoriasis and *menstruation*. At times it disappears during *pregnancy*. Balmanno Squire has especially drawn attention to this fact. One of our patients stated that she was free from psoriasis during each of her five pregnancies.

On the other hand, in some cases exacerbations have occurred, or psoriasis has been uninfluenced during the whole of pregnancy. *Lactation* has pretty regularly aggravated the eruption in some cases (McCall Anderson and Henry), but this does not point to any relationship between the two, as McCall Anderson and Wutzdorff seem to think. If there is any explanation at all, it is rather that pregnancy exerted a temporary favorable influence in such cases, and when over psoriasis relapsed.

*Relation of psoriasis to mental emotion.*—In several cases (Fournier, Heube, Leloir) acute psoriasis has appeared, usually after an interval of a few days, in consequence of severe shock, more rarely of anger. It has also been observed after more persistent mental disturbance.

Such cases French writers especially have insisted upon as showing a causal connection between mental disturbance and psoriasis. But as it is only a question of temporary coincidence there is no clear proof, but only a possibility of the existence of such a relationship ; in any case, it is of no value etiologically. No such evidence could be obtained in those cases where we made careful inquiry.

*Relation of psoriasis to the seasons.*—It is not uncommon to find that psoriasis of some years' duration, in a certain part of its course, regularly undergoes exacerbations and remissions at certain seasons. One of our patients (a male, aged thirty-seven) had, when twenty years old, extensive psoriasis which disappeared on treatment with baths, but reappeared regularly every spring and autumn, though in a slighter degree. When he was thirty he had typhoid fever in the autumn, and had no psoriasis that season ; it, however, recurred the following years at the same seasons. Fifty-six of our patients stated that they had almost regularly suffered from outbreaks at certain times of the year. The exacerbations took place most frequently in the spring, viz. 30 times (in conjunction with the autumn 12 times), in the autumn 10 times (excluding the previously mentioned 12 times), in the summer 10 times, and in the winter 6 times.

One case only is mentioned where a remission in the spring thus bearing out the above statement. This was a patient who had psoriasis for twenty-two years which dis-

appeared regularly at the end of March (before the bathing season), and remained away the whole of the summer. The remission was stated to have occurred twice only in the autumn, 11 times in the winter, and 22 in the summer. In ten cases the remission occurred during sea bathing, and conversely in one patient psoriasis was always aggravated by it.

There is no doubt, therefore, that a certain connection does subsist between psoriasis and the seasons, it being always worse in spring and in autumn. In two sailors psoriasis always improved when they were in hot climates.

*The geographical distribution of psoriasis.*—Psoriasis is usually stated to be *pandemic*. It is, however, questionable whether, according to Hirsch, the affections described under the various names of *gune* in Polynesia, *daud* in Assam, *curúba* among Brazilian Indians, are really psoriasis. Among negroes psoriasis is said to be rare (Morison); among Jews, on the other hand, frequent (Balmanno Squire). In very northerly latitudes it is not infrequent; thus in Iceland (Finsen) out of 513 cases of skin disease 42 were psoriasis (8·1 per cent.); scabies alone was more frequent (46 per cent.).

*The proportion of cases of psoriasis to those of other skin diseases.*—From a compilation of statistics collected from several of the larger towns in Europe we found that out of 15,376 cases of skin disease there were 993 cases of psoriasis, *i. e.* 6·5 *per cent.* The proportion, therefore, of psoriasis to other skin diseases was as 1 *to* 15. Similarly the gross statistics in North America (J. White) show that out of 58,617 cases of skin disease there were 1924 cases of psoriasis, *i. e.* 3·28 per cent. Thus it would appear that psoriasis occurs more frequently in Europe than in North America.

From a study of statistics psoriasis stands close in point of frequency to the most common parasitic skin diseases (dermatomycoses and zoonoses), and together with these (and acne) come next to eczema.

## III. Pathogenesis of Psoriasis.

*Psoriasis as an eruption of a constitutional disease or of a specific blood infection.*—None of the various theories about psoriasis suffice to account for its pathology. Accordingly psoriasis has been viewed as the expression of an assumed diathesis (dartrous, rheumatic, &c.), or as a definite constitutional disorder (syphilis, malaria, &c.), or as an infection of the blood with a specific organism (*Penicillium glaucum*, "*epidermidophyton*," "*Lepocolla repens*"). Still certain *clinical and etiological relations*, which have been pointed out from time to time by various authors, may be adduced in favour of the theory that psoriasis is a constitutional disease, or at any rate *a chronic infective disorder*, as Kopp supposes. Among such conditions the following may be distinguished :—the diffuse and at times acute character of the eruption; its development and frequent relapses, possibly due to the effects of internal treatment; the appearance of psoriasis in several members of the same family (direct and indirect transmission) ; its relation to acute diseases (typhoid fever), and the influence of other irritants (the poison of syphilis and variola). Finally psoriasis may appear after injury and vaccination, starting from the seat of lesion where the specific virus has effected an entrance into the blood. None of the above conditions are conclusive ; in fact, they may be used in support of other theories of psoriasis.

Inoculation experiments made with scales of recent psoriasis, which Destot[1] carried out on his own person, gave the following results. In fourteen days an ordinary pimple appeared at the site of inoculation in the right upper arm, and three distinct spots of psoriasis appeared over the elbow. He had never previously had, nor was there any hereditary predisposition to, psoriasis. As, however, the psoriasis did not manifest itself at the site of inoculation—in this the only case in human beings where inoculation was successful—this fact may be used in favour of the above theory. Unfortu-

[1] Destot and Augagneur, "Inoculability of Psoriasis," 'Mém. et Compt. rend. de la Soc. des Scienc. Méd. de Lyon,' vol. xxix, 1889, 2nd part; 'Compt. rend.,' 1890, pp. 131–3, 215–16.

nately, so far, this experiment stands alone; and besides, the exact details of the inoculation were not stated.

The cardinal objection to the general infection theory of psoriasis is the conspicuous absence of those clinical characteristics which mark infective diseases. *Psoriasis is in fact, in its whole nature, a skin disease pure and simple;* no psoriatic affection of mucosæ has been demonstrated which might support this theory, just as little as there are no pathological changes in other organs that could be considered of the nature of an irruption of a specific virus comparable to the eruption on the skin. In short, as already mentioned, there are no complications that have a direct relation to psoriasis. The disease is unaccompanied by fever; in a few cases (*v. supra*) slight subjective disturbances were stated to have been present, but these probably depended upon individual idiosyncrasy: an actual rise of temperature was never demonstrated. Finally, the general health does not suffer, as some writers have stated. Sometimes in cases of psoriasis inveterata, and more particularly in those with a character of dermatitis exfoliativa the general health is affected; but this is probably due to the universal implication of the skin, and not to the psoriasis as such, for we find similar disturbances of the general health when a local skin disease (*e. g.* favus) generalises.

Hence, in spite of the apparent support certain conditions lend to such a view, it is improbable that psoriasis is a constitutional disorder.

*Psoriasis as a neuropathic disease.*—Whilst several earlier writers (Tilbury Fox, Weyl, Lewin) have viewed psoriasis as a neuropathic affection from the symmetrical distribution of the efflorescences, its appearance after pregnancy, &c., Polotebnoff[1] has recently brought forward fresh evidence in support of this view, insisting on the presence of joint affections in psoriatics. In fact, his statements do not differ materially from those of Bourdillon.

Both these observers have found that psoriasis is only seldom inherited (3 out of 64 cases), but nervous affections are of frequent occurrence in the relations of the patient. According to them, psoriasis is seldom the chief process, a

[1] "Psoriasis," 'Monatsh. f. prakt. Dermat.,' supplement 1, 1891, pp. 141–2.

neurotic tendency is transmitted, and the psoriasis is one of the manifold signs of the disease—a vaso-motor neurosis. Polotebnoff says he has found various forms of nerve disturbance in psoriatics, and, like Bourdillon, includes joint affections. Certain objective nerve phenomena have also been emphasised. Rendu found in some cases of psoriasis circinata blunted sensation, and more or less definite analgesia even in healthy skin regions. Polotebnoff discovered analgesia in two psoriatics (alcoholics) : in one it only lasted a day ; in the other it was confined to isolated patches and their immediate vicinity. The application of electricity yielded very varying results. Among other points, the relation of psoriasis to mental emotion has been put forward as well as its chronic course, with tendency to frequent spontaneous remissions, the remedial action of arsenic, and the symmetry of the eruption.

Several other French writers (Besnier, Doyon, Brocq) assume a certain relationship between psoriasis and the nervous system, based upon their views of athropathies in general.

As regards these various considerations, as we have already mentioned, in none of our patients was any nervous affection shown to be at all frequent, and on the whole, only very few clinicians have been able to support the neuropathic theory. Even after examination of those of our patients who had joint troubles we could not make out any connection between psoriasis and the nervous system (*v. supra*). The relation of psoriasis to mental emotion is but based on an accidental periodicity, and this very same point has been adduced in favour of a similar relation in the case of favus and pityriasis versicolor, in which there can be no doubt whatever about a purely accidental coincidence. Moreover the various disturbances of sensation observed by some writers in psoriatics may in part be referred to the infiltration of the skin and to other complications (alcoholism and other neuroses), without any special relation to psoriasis, as they are often met with in regions free from efflorescences. In several cases where we specially looked for such a connection we were unable to find any evidence at all. Many of the points Polotebnoff adduces appear to rest on physiological considerations as much as on anything else, *e. g.* acceleration of the heart's action through psychic and physical disturbance, difference

of temperature of corresponding regions of the body, hyperidrosis of the axilla, &c. In short, there is scarcely an organ in which he has not found some vaso-motor disturbance in psoriatics. The usual symmetrical distribution of the efflorescences is so common in skin diseases of diverse origin—even parasitic (scabies and extensive pityriasis versicolor)—that this fact can scarely be used in support of the neuropathic theory of psoriasis. It is strange that Polotebnoff regards psoriasis as seldom hereditary, for most writers, including ourselves, have found heredity of weight as an etiological factor.

None of the above considerations seem to claim our adhesion to this theory, which certainly does not accord with the slight influence psoriasis has on the general health, with its chronic and indeterminable course, or even with the beneficial effects of arsenic at times. On the other hand, purely local treatment gives better results than arsenic; the relation of psoriasis to the seasons, the favorable influence at times of acute and chronic diseases, and its more frequent manifestation in males—especially after the twentieth year, although previous to this age there is no material difference in the two sexes—do not appear to bear out this theory, according to which we should expect the mucosæ as well as the skin to be affected. Again, although the relation of psoriasis to external irritants is regarded reflex in character, it is still inexplicable why an *interval of a week should elapse after the application of Köbner's experiment before there is any sign of efflorescence* in the scratch-mark. Still less does this theory explain those cases in which psoriasis, with no hereditary taint and after totally insignificant external causes, especially after vaccination, even when unsuccessful, manifested itself some days afterwards at the seat of inoculation. Bourdillon's statement that a thickening and shedding of the epidermis often result from nerve lesions proves nothing, for the simple reason that psoriasis is of quite a different nature; besides, no one has recorded a case of psoriasis appearing after a nerve lesion. From none of the numberless examinations of the nerves in psoriasis patches (Leloir, Vidal, Neumann, Kromayer, &c.) has any pathological evidence been forthcoming that will support such a theory.

We may conclude, therefore, that a neuropathic origin for psoriasis is not probable.

*Psoriasis as an idiopathic affection.*—Several of the older writers (Cazenave) regarded psoriasis as a substantive disease of the skin, often hereditary, and sometimes acquired only after certain profound changes in the skin due to other diseases, *e. g.* infectious diseases. F. Hebra and O. Simon apparently entertained this view, and compared the hereditary character of psoriasis with the black skin of the negro and congenital nævi. Köbner's experiment—psoriatic efflorescences appearing at the site of irritation—forced the older authors to admit a predisposition on the part of the skin—a psoriatic diathesis to develop psoriasis under various external and internal causes. According to Köbner, this diathesis was often hereditary, sometimes acquired, and might remain latent for an indefinite period. In this way he accounted for the sites of predilection, the temporary results of local treatment, and the great tendency to recurrence. Later on, Wutzdorff developed this theory, always assuming a congenital predisposition of the skin.

This theory rests only on the relation of the disease to irritation (external and internal), and on its assumed hereditariness. There are several grounds for objection to it. For there are diverse forms of irritation, varying in intensity, that play an important part in the evolution of skin diseases of widely different origin (urticaria, lichen ruber, syphilis, variola, scabies, favus, &c.), and therefore no great weight need be attached to such a causal relationship to psoriasis. This skin diathesis, further, is not peculiar to psoriasis, for these patients may get other skin diseases (eczema, dermatitis), and, as a rule, are just as susceptible to other skin affections as other people. Further, the hereditariness of psoriasis is not proved, and even in the light of the most favorable statistics such an hereditary disposition does not obtain even in half the cases on record. The fact that psoriasis, in spite of repeated traumatism even in hereditary cases, occurs as a rule only several months after birth, can only be referred, like the long periods of remission, to some unknown latent condition. This theory does not explain the punctiform and late appearance of the efflorescence in

Köbner's experiment, the scattered macular eruption, the growth of the rash, &c. Thin, who supports Köbner's theory, rather accounts for the peripheral growth of the eruption by an infective process spreading to the neighbouring cells. This theory distinctly approaches that of local parasitism. The weak point is that we know nothing of the nature of the skin proclivity to such parasitism. We can only state that the patient who has or gets psoriasis shows this proclivity. This diathesis is not, therefore, unlike the *diathèse dartreuse* which is regarded as conditioning psoriasis.

*Psoriasis as a parasitic affection.*—Some of the older writers have hinted at this supposition, but it was Lang who first formulated it. In the first place[1] he showed from its clinical characters a similarity to other know dematomycoses; then[2] he found the presence of a presumed fungus (*epidermidophyton*) constant in psoriasis scales. Lastly,[3] he published remarkably favorable results of antiparasitic treatment, though carried out in very few cases. These statements of Lang's gave rise to a series of investigations upon the nature of the fungus; some (Eklund, Beissel, Wolff) yielded positive, others (Neisser, &c.) negative results. De Matei, on the other hand, discovered a micrococcus which he considered was the cause of psoriasis. These researches, however, fell to the ground when Ries demonstrated that the presumed fungus of Lang was an artificial product. Since then no other specific micro-organism has been found.

Attempts have been made by *inoculation experiments* on animals[4] and man to verify the parasitic theory. After inoculating rabbits, efflorescences resembling psoriasis appeared in some cases (Lassar, Tommasoli) in other cases;

[1] "An Attempt at a Classification of Scaly Affections according to their Clinical Characters," 'Vierteljahressch. f. Derm. u. Syph.,' 1878, pp. 433–44.

[2] "Preliminary Communication of a New Discovery in Psoriasis," ibid., 1879, pp. 257–63.

[3] "The Treatment of Psoriasis," ibid., 1880, pp. 473–85; cf. "Psoriasis" in Volkmann's 'Collection of Clinical Essays,' No. 208, 1881, pp. 1765–88.

[4] It is very doubtful whether psoriasis ever occurs in animals. Several veterinary pathologists (Prof. Bang, Friedberger, Fröhner) state they have never observed it in domestic animals. In some instances (Höring, Hafner, Janzer, Tenholt) of accidental communication of psoriasis from animals to man it would appear that it was, after all, herpes tonsurans.

accounted for by the dissemination of the fungus. In these particulars psoriasis is in complete harmony with other dermatomycoses. No other theory accords so well with the distribution of the eruption, now in grouped aggregations, now as satellites to extensive patches, or again in a serpiginous form, due to the confluence of contiguous circles.

Lang accounts for the *sites of predilection* by referring to the natural characters of the skin which favour the development of the fungus. The skin over the elbows, knees, and shins is frequently thickened, somewhat rough and furfuraceous. External irritation (pressure and friction of the clothes, &c.), which goes to produce such a condition of the skin, has always a most important bearing on the localisation of psoriasis as well as in other parasitic diseases, if not to quite the same extent. However, the localisation of these diseases is not always the same, probably because the different (anatomical and physiological) characters of the skin, *i. e.* the soil, are determined by the different regions (flexor and extensor surfaces), and, above all, by varying conditions of life. Thus favus (F. Hebra, Kaposi), besides attacking chiefly the scalp, may also like psoriasis, and unlike dermatomycosis circinata, affect the extensor aspect of the extremities and the trunk. Symmetrical distribution of the eruption occurs in well-recognised parasitic diseases (scabies, dermatomycosis circinata) just as definite as in psoriasis, and is readily explained by anatomical and physiological considerations which offer a similar soil for the development of the organism in connection with the usual bilateral external causes of irritation. The nails are attacked by mycoses just as by psoriasis, and, as Lang points out, the diseases are analogous (cf. Kaposi, &c.). The palms, according to Lang, are as rarely affected with psoriasis[1] as with other dermatomycoses, and the mucosæ are never attacked.[2] Psoriasis must, therefore, be regarded as a purely local affection ; and, just as is the case with other dermatomycoses, no internal

[1] As above mentioned, this localisation is not after all so seldom as is usually stated, and the same may possibly hold good in *Trichophyta palmæ* (cf. ' Monatsh. f. prakt. Derm.,' 1887, No. 23, abstract from " Congress in Pavia," Pellizari).

[2] Kaposi has seen a remarkable and unique case of favus where the autopsy showed favus foci in the mucosæ of the œsophagus and stomach.

disease can be shown to have any share in its causation. From a pathological point of view no objection can be urged against this theory, and in respect to sex and age nearly similar conditions hold good for psoriasis as for favus and dermatomycosis circinata. The difference in point of frequency of the sexes affected with psoriasis is probably due to the greater exposure of males to infection. Favus also occurs more in males than in females. Lastly, psoriasis resembles other dermatomycoses in its irregular distribution, in its relation to the seasons, and in its relative frequency compared with other diseases of the skin.

Among circumstances apparently antagonistic to this view Lang cites *heredity*, which he rather regards as a predisposing factor. It is well known that the transmissibility of a parasitic disease, under the ordinary conditions of life, depends on the nature of the soil, *i. e.* the skin, and varies greatly in different people even under the same conditions. But as psoriasis occurred most frequently in the patient in whom there was direct heredity, and somewhat less so in two or more of the same offspring—circumstances which do not of themselves support the hereditary character of the disease—we may also assume that there is a predisposition on the part of the skin (a more suitable soil for the development of the fungus) which is inherited, and may possibly be not of infrequent occurrence. In fact, we assume exactly those conditions which we believe to exist in the integument of a person liable to any parasitic affection. As regards the second and equally important factor in parasitic skin diseases, viz. the *source of infection*, it is close at hand where parents or relatives of the patient are affected with psoriasis. As already mentioned, it begins much more frequently in those children where the disease is in the direct line of descent than in others. If it is really a question of infection, and not heredity, we ought then to meet with cases where the parents have been attacked after the children—a possibility which has hitherto never received any consideration. In one of our patients actually the mother had psoriasis for the first time long after the daughter. But as psoriasis manifests itself more frequently in early age, such cases must always be few and far between.

It has been urged against the parasitic theory that no case is on record where infection took place between individuals living under the same conditions and not related, *e. g.* between married persons. Lang refers this circumstance to the absence of skin predisposition, and cites in evidence of this the exceeding rarity of infection of pityriasis versicolor, where actually the fungus abounds in the superficial layers of the epidermis. Even in favus where several members of the family use the same comb and brush, they have escaped infection.[1] Further, Lang thinks that once attention has been drawn to the question of infection, such cases will probably be found; but if psoriasis be viewed *a priori* as non-parasitic, cases illustrating a possible etiology of infection will be either overlooked or explained away. In spite of neglect of observation we have been able to collect several cases in which infection was probable. At the Congress of 1884, held in Copenhagen, Dr. Unna communicated a case where three children without any family history developed psoriasis in quick succession, shortly after a nurse suffering from it had been engaged. Among our private patients a similar case occurred, but only one child was affected. In six of Poor's cases[2] (66 hereditary cases) psoriasis was present in both parents, and in one of our cases both maternal grandparents had the disease. Hammer[3] records a case where father and daughter were treated at the same time for a primary attack of psoriasis from which the mother and aunt had suffered for some time. One of McCall Anderson's[4] patients was attacked with psoriasis whose wife had suffered for years from the disease. Aubert[5] relates two cases where the husband had psoriasis and the wife developed it later on. A patient of Augagneur's[6] suffering from trade eczema developed psoriasis in the eczematous region, have occupied a

[1] This has frequently been pointed out in the Annual Reports of the General Hospital, Copenhagen. Formerly, indeed, the infectiousness of favus was explained by heredity (Alibert).

[2] 'Schmidt's Annual,' vol. lxxviii, 1878, p. 148.

[3] "Psoriasis Vulgaris," 'Transactions of the Medical Clinic,' Würzburg, vol. ii, 1886, pp. 404–5.

[4] 'Psoriasis and Lepra,' 1865, p. 37.

[5] "Discussion on the Inoculability of Psoriasis," Destot and Augagneur, loc. cit., p. 132.

[6] Ibid.

bed in the hospital for four months between two psoriatics. Similarly another patient showed psoriasis on the site of an artificial dermatitis. As these cases are adduced in support of the parasitic theory, we must assume that psoriasis appeared then for the first time, although it is not expressly stated.

Lastly, Dr. Beissel[1] gives particulars of two brothers who went on their travels together, and of two cousins who occupied the same bed, where psoriasis appeared for the first time shortly after. These cases are perhaps of not so much value, on account of the relationship of the patients; moreover the grandfather of the two cousins suffered from psoriasis. The patients themselves sometimes state they have caught the disease. One of our patients maintained he had got psoriasis—first attack on the shins—through wearing the trousers of another man suffering from it; such statements naturally should be received with caution. All the above cases of infection are proportionately few in number; still, in conjunction with the other circumstances stated above, they throw doubt upon the theory of heredity, and certainly urge us to further researches in this direction.

Lang explains the presence of psoriasis appearing sometimes at the *seat of irritation* by inoculation on a soil that has thus been suitably prepared. He cites the analogous instance of the dissemination of the dermatomycoses through scratching (favus, Aubert). Inoculation of irritated or previously diseased regions (eczema) may be presumed to be much easier in parasitic diseases when not only the parasitic elements are present in the efflorescences, but actually scattered over the healthy skin, *e. g.* in a case of extensive favus (Kaposi). Where scratch-marks are the sites of the eruption, which are not rare in psoriasis, and are often seen in ecthyma and impetigo contagiosa (Fox), it is only natural to conclude that the nails have effected the inoculation. But what renders this more probable is Köbner's experiment, which, strange to say, Lang does not sufficiently accentuate. The scratching is quite superficial, does not extend to the dermis, and no bleeding takes place. The efflorescence only appears during the evolution of psoriasis,

[1] 'Aix-la-Chapelle as a Health Resort,' 1889, p. 130.

and not always then, especially when several scratches are made. The spots appear in the course of eight to ten days, never later; they are punctate and situated in the scratch itself. These circumstances, *particularly the manifestation after a tolerably definite period* of incubation,[1] seem to show that an actual inoculation[2] has occurred. It is not probable that psoriasis should appear in this way were it related to a general blood infection. Köbner never succeeded in producing psoriasis efflorescences in syphilis; and certainly no other theory of pathogenesis affords so natural an explanation of this phenomenon.

In those infrequent cases where psoriasis was manifest *for the first time in irritated areæ* (wet cupping, compresses, &c.—*v. supra*), *or in regions already diseased*, and where no "hereditary taint" was present, the parasitic theory offers the most reasonable solution. This holds good particularly in those case where a primary attack of psoriasis supervenes on *vaccination* (*v. supra*). The efflorescences appear at the site of inoculation, either after the detachment of the seat or in the course of a few days in cases of unsuccessful vaccination, and subsequently spread acutely. In two cases at least Rohé expressly states that there was no history of psoriasis. It may be objected that animal lymph was used, and that

[1] Köbner ('Klin. u. experim. Mitth. aus d. Derm. u. Syph.,' Erlangen, 1864, p. 23) discovered on inoculation of human beings with *Trichophyton tonsurans* that the eruption appeared in four to five days, in rabbits about eight days. Several days also were required for the development of *Achorion Schönleinii*.

[2] If this theory be correct we should not expect any efflorescences to develop if Köbner's experiment is conducted under rigid antiseptic precautions.

We have performed Köbner's experiment in three different ways on some few occasions. The methods were carried out on the same patient. In the first method scales were rubbed into the scratch; in the second this was not done; in both the skin was previously rendered antiseptic, and sterilised cotton wool applied. The third method was carried out without any antiseptic measures except the after-application of a pad of antiseptic wool. The result was negative in all three methods. Further experiments may of course be successful, but isolated positive results do not prove anything, for even under ordinary circumstances an efflorescence is only developed in one of two simultaneous scratches. Such experiments must be carried out in large numbers in patients preferably not undergoing treatment, and where the psoriasis is in the evolution stage.

psoriasis scarcely occurs in calves. The source of infection, however, cannot always be traced, as Hager[1] has shown in epidemics of herpes tonsurans (or impetigo contagiosa) which appeared at the site of inoculation immediately after vaccination with animal as well as human lymph.

As the liability to parasitic skin affections varies with different persons, so probably in the same person transient, and especially (persistent) *disturbances of nutrition of the skin* must largely influence this proclivity. Lang sees in this circumstance, as Köbner previously stated, an explanation of the curative influence which other diseases accompanied by profound tissue change or by fever exert over psoriasis. After cessation of such disturbances the eruption usually returns. Parasitic diseases like favus, scabies, are analogous examples. It is not uncommon for dermatomycoses like psoriasis to disappear spontaneously. From such a standpoint we may account for the retrocession of psoriasis during pregnancy, its return during lactation, as well as the influence which alteration in the habits of life often exerts over the disease. As regards the deteriorating effects of alcoholism and rheumatism on psoriasis, we shall not be far wrong in maintaining that the skin is rendered more suitable for the development and growth of the organism, just as we rightly assume that certain conditions increase and certain others decrease its sensitiveness.

Against Lang's theory it has been urged that psoriasis may disappear upon *internal treatment* only. Lang makes the remark that in such cases the arsenic, even in such small quantities, in the blood may act antiparasitically,[2] as is the case with large doses of iodide of potassium, thus rendering the skin no longer a favorable medium for the propagation of the organism. Moreover internal treatment alone is not by any means successful, and it is almost always combined with external measures, which are nowadays regarded as the most reliable. Brocq[3] states that formerly internal treat-

[1] "Animal Lymph and Herpes Tonsurans," 'Berl. klin. Wochenschr.,' March 5th, 1888, p. 197.

[2] Unna ('Vierteljahresschr. f. Derm. u. Syph.,' 1880, p. 550) puts forward the same supposition in a case of psoriasis gyrata cured externally with an ointment of vaseline containing potassium arsenite (1 in 30).

[3] 'Treatment of Diseases of the Skin,' 1890, p. 704.

ment was everything, whereas to-day it has fallen into disrepute. The most effective external remedies are indeed those we view as *antiparasitic* in action—chrysarobin[1] and tar preparations. Lang especially has employed antiparasitic remedies, laying particular emphasis on the method of application, and retaining the patients in hospital some time after all trace of psoriasis has disappeared. The results of his treatment were materially better as regards permanency of cure and absence of relapse than those obtained by the usual methods, where, as a rule, not so much importance is attached to the complete disappearance of every efflorescence before the patient is discharged. Further, psoriasis is stated by other writers (Devergie, Brocq, Eichhoff, Schultz) to be much less liable to relapse after external treatment when every trace of it has been removed. But satisfactory investigations in this direction have still to be made.

Meanwhile the constant tendency to *relapse* and the *implied incurability* of psoriasis militate against this theory; but, as Lang pertinently remarks, pityriasis versicolor, as is well known, is most frequently subject to relapses even after repeated treatment. Bienstock[2] believes that it is quite possible that infective fomites exist on the sound—and therefore untreated skin—and cause the relapse. He therefore considers it advisable, as is done in the dermatological clinic in Breslau, to submit the whole skin to treatment with mild salicylic acid and β-naphthol ointments for several weeks after the psoriasis has been cured. In certain cases the occasional return of psoriasis to the same regions after long intermission, and apart from the predilection sites, may possibly be accounted for by the persistence of spores (in the epidermic layers ?). Hardy makes this assumption in dermatomycoses, which recur after weeks' or even months' apparent cure. The most probable reason of these constant relapses, according to this view of its pathogenesis, is *that treatment has never been carried out so thoroughly as in cases*

[1] Bienstock sees in the curative action of chrysarobin, pyrogallic acid, and anthrarobin a further proof of the parasitic nature of psoriasis. These drugs absorb oxygen, and so bring about the death of the fungus.

[2] "Therapeutics of Psoriasis," Inaugural Dissertation, Breslau, 1888, pp. 34–5.

*of known parasitic disease.* No great weight has been attached to the importance of removing every trace of psoriasis, of keeping the patient under observation for some time after, as in favus, and certainly *not of disinfecting* the clothes, bedding and toilet articles (brushes, comb, &c.), as is the generally followed routine method with scabies and favus. Lang, who relegates the skin proclivity to the background, does not accentuate the importance of such details. Another feature, and one which has hitherto escaped notice, is the not infrequent presence of psoriasis in other members of the family, and the liability to reinfection owing to the assumed existence of the parasite apart from the skin in a susceptible patient. These considerations are in themselves sufficient to explain the frequent relapses, a characteristic which is almost indispensable to the correctness of the theory, even where there have been complete intermissions, lasting in some cases for many years. Of course it is still open to question whether these are really intermissions, or not, after all, remissions with a few persistent spots in the predilection sites that may have escaped notice.

*Hence we should not lay it down as an absolute rule that psoriasis is incurable,* and, as Lang states, cases of definite cure have been recorded; on the other hand, in the light of the above-mentioned statements about intermissions of several years' duration, no great value should be attached to such records.

Although we have no real proof for the parasitic theory, still Lang's statements, which we are in a position to confirm and materially to supplement, establish *its probable correctness,* be the causes either hyphomycetes or schizomycetes. In reviewing the other theories of psoriasis it is evident that several important points remain either inexplicable, or their solution is sought in various dubious relations between psoriasis and other diseases. The pathogenetic theory which in comparison with others best meets the arguments is that of psoriasis being a general infectious disorder. It must, therefore, agree in its main features with local parasitism. The fact that there are not many adherents to this view is probably explained by the non-success of researches for the micro-organism, the firmly rooted impression of heredity,

and the incurability of psoriasis. On the other hand, sufficient weight is not attached to the condition of the nutritive medium, *i. e.* the skin, when the question of parasitism arises. For not only does this condition vary in different persons, but even in the same person, and depends necessarily on tissue change as a whole, and its effects may be quite unlooked for. These circumstances have not been sufficiently studied hitherto. Were it not that the parasite in pityriasis versicolor is well known, as Lang has more than once pointed out, more objections could be urged against the parasitic causation of it than in the case of psoriasis.

The chief practical result of this theory is the employment of energetic antiparasitic treatment (especially chrysarobin, tar preparations, &c., in conjunction with baths) applied locally as Lang recommends. Internal treatment (arsenic and iodide of potassium) must be viewed under certain conditions only as an auxiliary measure, and possibly as expediting cure. At all events, every trace of eruption should be got rid of, and, as Bienstock advises, the whole skin itself should be afterwards treated, and the patient kept under observation for some time. In order to prevent any possible reinfection, the clothes, bedding, and all articles that might harbour fomites should be thoroughly disinfected. Even then in cases where the patient's relations suffer from the disease, and are living under the same roof, reinfection may take place unless they are submitted to similar treatment. It is only when the treatment and precautions used in recognised parasitic diseases are employed that we may expect to cure psoriasis definitely, and without any chance of relapse.

# INDEX.

*Although a tolerably detailed Index to Dr. Morrow's paper on Drug Eruptions has already been given (see p. 566) yet it has been thought it might serve the reader's convenience to give here a brief General Index to the contents of the volume as a whole.*


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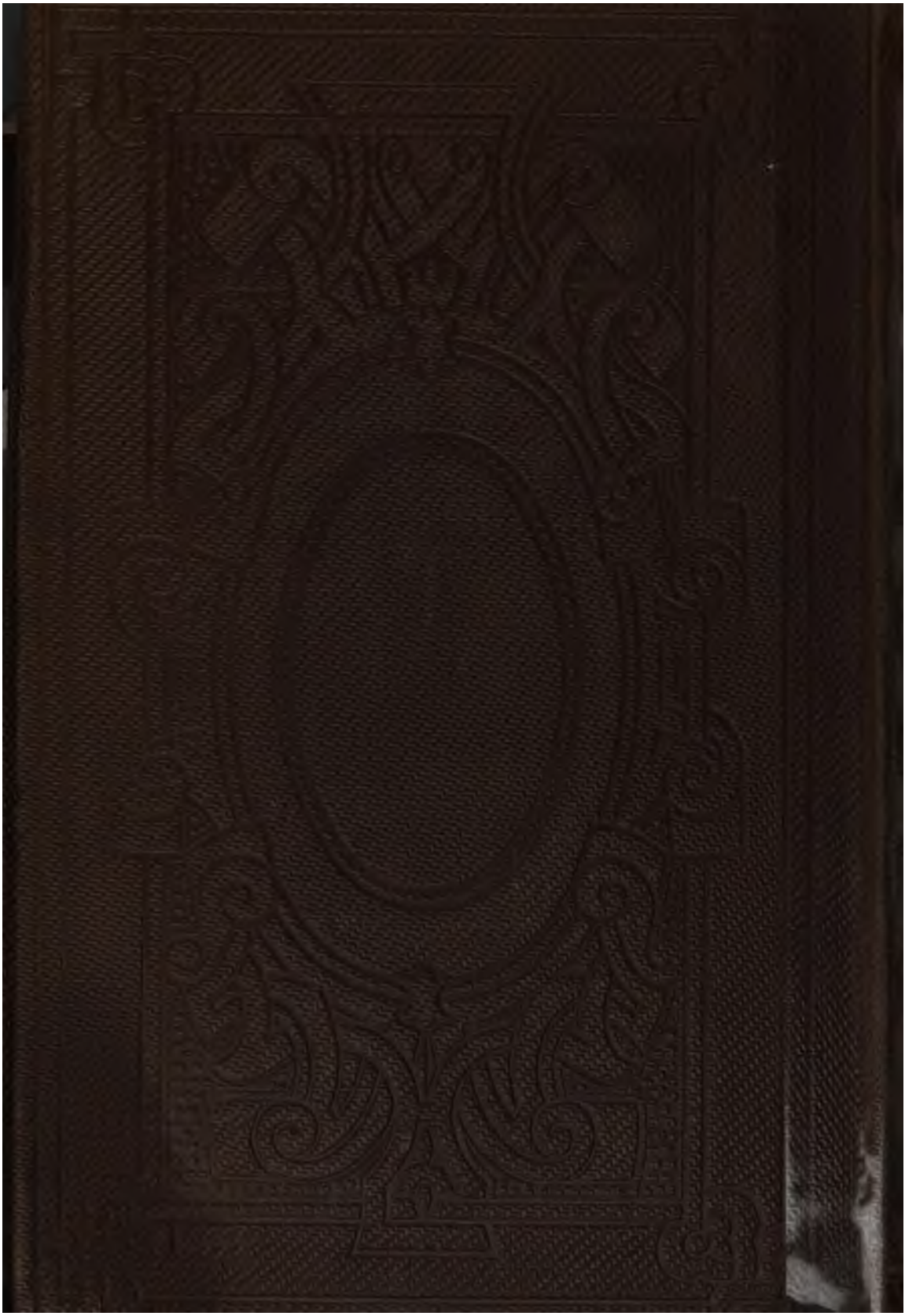
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